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AUGUST—*Continued*

|   | PAGE |
|---|------|
| Vincent's Disease of the Skin    Albert Strickler, M D, Philadelphia  | 87   |
| Lupus Erythematosus    Treatment with Oxophenarsine Hydrochloride    Captain Lawrence C Goldberg, Medical Corps, Army of the United States  | 89   |
| Erythema Multiforme    Report of a Case of Severe Erythema Multiforme with Involvement of the Mucous Membranes Treated with Penicillin    H C Robinson, M D, Grand Rapids, Mich                       | 91   |
| Allergic Reactions During the Administration of Penicillin    John Henderson Lamb, M D, Oklahoma City   | 93   |
| Penetration of Surface Tissues with Copper by Iontophoresis    Penetration with Organic and Inorganic Copper Salts and the Use of Detergents in Iontophoresis    Commander Armand J Pereyra (MC), USN | 96   |
| White Cross Striae of the Finger Nails Following Cardiac Infarction    Erich Urbach, M D, Philadelphia  | 106  |
| Classification of Tuberculosis of the Skin    Henry E Michelson, M D, and Carl W Laymon, M D, Minneapolis   | 108  |
| Extragenital Syphilitic Infection in Negroes    H H Hazen, M D, Washington, D C   | 114  |
| Clinical Notes  |      |
| Semblance of Elastic Tissue to Mycelium in Potassium Hydroxide Preparations    Walter S Green, M D, and Maurice C Shepard, M S, Greenwood, Miss   | 115  |
| Ringworm of the Eyebrow    Emanuel Muskatblit, M D, and Nathan A Targan, M D, New York  | 116  |
| Correspondence  |      |
| One Hundredth Anniversary of the First American Textbook of Dermatology    James Quincy Gant Jr, M D, Bethesda, Md  | 117  |
| Vitamin B Complex for Vitiligo    J C Hathaway, M D, Spokane, Wash  | 117  |
| Obituaries  |      |
| John Harper Blaisdell, M D  | 119  |
| Abstracts from Current Literature   | 120  |
| Society Transactions  |      |
| New York Dermatological Society   | 123  |
| San Francisco Dermatological Society  | 129  |
| Manhattan Dermatologic Society  | 132  |
| New England Dermatological Society  | 136  |
| Los Angeles Dermatological Society  | 141  |

## SEPTEMBER 1945    NUMBER 3

|  |     |
|--|-----|
| Intensive Arsenotherapy of Early Syphilis    Loren W Shaffer, M D, Detroit   | 147 |
| Intensive Treatment of Early Syphilis with Oxophenarsine Hydrochloride by Multiple Injections    E J Trow, M D, and H A Dixon, M D, Toronto, Canada  | 155 |
| Onychomycosis and Dermatomycosis Caused by Trichophyton Rubrum and Aspergillus Nidulans    Major Eugene S Bereston, Medical Corps, Army of the United States, and First Lieutenant William S Waring, Sanitary Corps, Army of the United States | 162 |
| Undecylenic Acid in the Treatment of Dermatomycosis    Arthur L Shapiro, M D, and Stephen Rothman, M D, Chicago  | 166 |

SEPTEMBER—*Continued*

|  | PAGE |
|--|------|
| Polycythemia with an Unusual Eruption    Albert Strickler, M D, Philadelphia   | 172  |
| Creeping Eruption    Results of Treatment with Fuadin    Captain Frank A Dolce and<br>Major John E Franklin, Medical Corps, Army of the United States                                | 174  |
| Xeroderma Pigmentosum    Additional Notes on the Six Cases of Dr Mayrand and<br>Dr Gaumond    Madge Thurlow Macklin, M D, London, Ontario, Canada                                    | 176  |
| Treatment of Ichthyosis    Captain Hyman H Gordon, Medical Corps, Army of the United<br>States   | 178  |
| Colloid Degeneration of the Skin (Colloid Milium)    Report of a Case, with Observations<br>on Ascorbic Acid Therapy    Saul S Robinson, M D, and Samuel Tasker, M D, Los<br>Angeles | 180  |
| Clinical Notes   |      |
| A Failure of Penicillin in the Treatment of Granuloma Inguinale    Report of a Case<br>Captain John R Haserick, Medical Corps, Army of the United States                             | 182  |
| Obituaries   |      |
| James Thomas Wayson, M D   | 183  |
| Correspondence   |      |
| Penicillin in the Treatment of Cutaneous Diseases    Captain Lawrence C Goldberg,<br>MC, A US  | 184  |
| Treatment of Pityriasis Rosea with Trichophyton Extract    Lieutenant Commander<br>C C Carpenter (MC), USNR  | 184  |
| The Effective Three Hour Treatment of Scabies    Maurice Oppenheim, M D,<br>Chicago  | 184  |
| The Use of Methenamine in Dermatology    Hyman I Goldstein, M D, Camden, N J   | 185  |
| Abstracts from Current Literature  | 186  |
| Society Transactions   |      |
| Philadelphia Dermatological Society  | 189  |
| Metropolitan Dermatological Society  | 192  |
| Chicago Dermatological Society   | 194  |
| New York Dermatological Society  | 203  |
| New York Academy of Medicine, Section of Dermatology and Syphilis  | 210  |
| Manhattan Dermatologic Society   | 214  |
| Book Reviews   | 219  |

## OCTOBER 1945    NUMBER 4

|  |     |
|--|-----|
| A New Cutaneous Syndrome Occurring in New Guinea and Adjacent Islands    Prelimi-<br>nary Report    Major Thomas N Nisbet, Medical Corps, Army of the United States  | 221 |
| Clinical Investigation of a New Cutaneous Entity    Lieutenant Colonel Charles L Schmitt,<br>Medical Corps, Army of the United States, and Major O Alpins and Captain George<br>Chambers, Medical Corps, Australian Army | 226 |
| Beta Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Treatment of<br>Urticaria    Arthur C Curtis, M D, and Betty Brechner Owens, M D, Ann Arbor,<br>Mich  | 239 |
| Use of Benadryl for Urticaria and Related Dermatoses    A Preliminary Report    Loren<br>W Shaffer, M D, Lee Carrick, M D, and Herschel S Zackheim, M D, Detroit   | 243 |

OCTOBER—*Continued*

|   | PAGE |
|---|------|
| Penicillin Ointment Studies on Stability Relative to Potency and on the Sensitivity of the Human Skin to Patch Tests with Ointment Lieutenant Commander Ralph B Coomber (MC), U S N R | 246  |
| Diseases of the Skin Among the Natives of Northeast New Guinea Captain William D Wolfe, Medical Corps, Army of the United States  | 247  |
| Sensitivity of the Tuberculin Patch Test (Vollmer-Lederle) Results with Three Hundred and Eighteen Persons Presenting Various Dermatoses Kurt Loewenthal, M D, Brooklyn               | 249  |
| Effect of Feeding a Lipotropic Substance to Patients with Xanthelasma Arthur C Curtis, M D, and John P Berger, M D, Ann Arbor, Mich   | 252  |
| Relation of Ultraviolet-Induced Mutations to Speciation in Dermatophytes C W Emmons, Ph D, and Alexander Hollaender, Ph D, Bethesda, Md   | 257  |
| Contact Dermatitis of Eyelids Caused by an Antioxidant in Rubber Fillers of Eyelash Curlers Report of Seven Cases Captain George H Curtis, Medical Corps, Army of the United States   | 262  |
| Scrotal Tongue and Its Inheritance Norman Tobias, M D, St Louis   | 266  |
| Clinical Notes  |      |
| An Improved Method for Preparing Permanent Slides of Fungus Cultures J Walter Wilson, M D, Los Angeles  | 267  |
| Correspondence  |      |
| Course in Tropical Dermatology Herbert Rattner, M D, Chicago  | 268  |
| Impetigo Bullosa in the Tropics Simon S Rubin, M D, Chicago   | 268  |
| News and Comment  | 269  |
| Obituaries  |      |
| Henry J F Wallhauser, M D   | 270  |
| Abstracts from Current Literature   | 272  |
| Society Transactions  |      |
| Los Angeles Dermatological Society  | 275  |
| Minnesota Dermatological Society  | 283  |
| Chicago Dermatological Society  | 287  |
| Philadelphia Dermatological Society   | 293  |
| Book Reviews  | 300  |

## NOVEMBER-DECEMBER 1945 NUMBER 5

|  |     |
|--|-----|
| Carbohydrate Metabolism and the Skin Erich Urbach, M D, and John W Lentz, M D, Philadelphia  | 301 |
| Epidermolysis Bullosa A Suggestion as to Possible Causation Captain Marvin N Winer and Captain Jack Morton Orman, Medical Corps, Army of the United States | 317 |
| Acne Vulgaris Occurring in the Tropics in a Pigmentary and Pilosebaceous Nevus Commander Herman V Allington (MC), U S N R                                  | 322 |
| Effect of Endocrine Substances on the Adult Human Scalp Hugo R Rony, M D, and Samuel J Zakon, M D, Chicago   | 323 |
| Epidermodysplasia Hystricoidis Bullosa Report of a Case with Histopathologic Study Jose G Reyes, M D, New York   | 328 |

NOVEMBER-DECEMBER—*Continued*

|  | PAGE |
|--|------|
| Dermatology in an Army Station Hospital Serving in Italy    Captain Emory Ladany, Medical Corps, Army of the United States   | 335  |
| Fixed Bullous Eruption Due to Sulfathiazole    James A McGuire, M D, and Bertram Shaffer, M D, Philadelphia  | 342  |
| Treatment of Dermatoses with Vasodilators    Frederick Rehm Schmidt, M D, Chicago  | 344  |
| Pigmentation of Hair on Transplanted Skin in Hooded Rats    Earl O Butcher, Ph D, New York   | 347  |
| Lichen Sclerosus et Atrophicus in Childhood    Carl W Laymon, M D, Minneapolis   | 351  |
| Differentiation of Lepromatous from "Neural" Leprosy    The Basis, a Method, and Report of Five Cases    Harry L Arnold Jr, M D, Honolulu, Territory of Hawaii   | 354  |
| Sandals, and Hygiene and Infections of the Feet    Lieutenant Walter J Nickerson, Sanitary Corps, Army of the United States, Lieutenant Colonel Laurence Irving, Air Corps, Army of the United States, and Major Henry E Mehmert, Medical Corps, Army of the United States | 365  |
| The Adrenal Glands in Pemphigus Vulgaris    Report of Six Autopsies and Review of the Literature    Joseph W Goldzieher, M D, New York   | 369  |
| Cutaneous and Subcutaneous Lesions of the Lower Limbs in Connection with the Veins    Differential Diagnosis    Max Wolf, M D, New York  | 376  |
| Dermatitis Venenata Following Use of Penicillin Ointment    Lieutenant Commander Leonard Simpson Markson (MC), U S N R   | 384  |
| New Cutaneous Bactericidal Agent—Used in Soap    Further Practical Studies    Eugene T Traub, M D, New York, and Chester A Newhall, M D, and John R Fuller, B D, Burlington, Vt  | 385  |
| Dermatitis Medicamentosa Associated with Secondary Polycythemia    Report of a Case    Saul S Robinson, M D, and Samuel Tasker, M D, Los Angeles   | 389  |
| Waterhouse-Friderichsen Syndrome    Report of a Case    Harold M Johnson, M D, Honolulu, Territory of Hawaii   | 391  |
| Colloidoclastic Shock Following Injection of Oxophenarsine Hydrochloride (Mapharsen)    Report of a Case    Arthur L Shapiro, M D, Chicago   | 395  |
| Carbarsone in the Treatment of Pemphigus    A Preliminary Report    Robert P Little, M D, New York   | 397  |
| Clinical Notes   |      |
| Fever and Sterile Abscess Formation Accompanying Treatment of Syphilis with Penicillin    M Edward Goebel, M D, and Arthur W Grace, M D, Brooklyn  | 399  |
| Erysipeloid Treated Successfully with Injections of Penicillin    Report of a Case    Maurice J Costello, M D, New York  | 400  |
| Correspondence   |      |
| Semblance of Elastic Tissue to Mycelium in Potassium Hydroxide Preparations    E Muskatblit, M D, New York   | 401  |
| Isaac R Pels, M D, Baltimore   | 401  |
| Demonstration of Effect of Nutrition on the Skin    Lieutenant Colonel J F McClendon, Nutrition Division, U S Army Reserve   | 401  |
| Obituaries   |      |
| Kendal Frost, M D  | 403  |
| Abstracts from Current Literature  | 405  |

NOVEMBER-DECEMBER—*Continued*

|                                       |      |
|---------------------------------------|------|
| Society Transactions                  | PAGE |
| Central States Dermatological Society | 413  |
| Cleveland Dermatological Society      | 423  |
| Metropolitan Dermatological Society   | 425  |
| News and Comment                      | 428  |
| Book Reviews                          | 429  |
| Directory of Dermatologic Societies   | 430  |
| General Index                         | 433  |

## A TROPICAL LICHEN PLANUS-LIKE DISEASE

LIEUTENANT COMMANDER JAMES W BAGBY, MC-V(S), USNR

Since the beginning of the war there have appeared on some tropical islands of the Pacific numerous cases of a disease which in its clinical appearance is suggestive of lichen planus. The total number and the percentage of personnel affected are impossible to estimate. That the number is large is obvious in this west coast Naval Hospital, which receives nearly all its patients directly from overseas. In the last eight months of 1944 about 25 cases of this disease have been observed here, 20 of them in the last three months.

According to the histories obtained, some of these eruptions begin as true lichen planus. In others, a generalized erythematous eruption, usually diagnosed as an exfoliative dermatitis, is followed by localized patches of the disease under consideration. In still others large areas of pustules develop, thought to be secondarily infected miliaria or impetigo, which in healing are replaced by lesions resembling hypertrophic lichen planus.

The distribution is usually generalized, with the extremities showing the heaviest involvement. In several patients the midportion of the trunk was strikingly free of lesions. In 1 of them the area of skin protected by a wristwatch and its band was free of involvement, although the entire forearm and hand were affected with the lesions of the disease. The face is usually involved. Several patients have had scarred patches in the scalp, producing what is apparently a permanent alopecia. Thickened grayish white patches on the tongue and oral mucosa are commonly though not invariably observed. I have seen no involvement of the glans penis, although the shaft and scrotum are involved in some. Hypertrophic lesions on the palms and soles are common, as are thickening, separation, ridging and discoloration of the fingernails and toenails.

Active lesions consist of papules and confluent papules and nodules. These are covered with a heavy, grayish, warty, adherent scale. When this is removed, the underlying area bleeds and has

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a brown to purple color. With regression of the disease the involved areas vary from those which are lightly pigmented a brownish color to atrophic, depressed, deeply pigmented scars. The tongue and oral mucosa, when affected, do not improve with the remainder of the eruption. In the initial stages of the disease itching is usually present and in a few patients this was described as severe. It is not as prominent a complaint as in the usual patient in the United States with typical lichen planus.

The 5 men whose cases are reported were admitted to this hospital from overseas on the same day.

## REPORT OF CASES

CASE 1—C I W, a 45 year old white man, had been in the tropics for four months prior to the onset of the disease. When the eruption began, he was on Bougainville. He had previously been on Guadalcanal, having arrived there directly from the United States. An attack of malignant tertian malaria had subsided after treatment with quinine and quinacrine hydrochloride a week before the skin became involved. Lesions appeared first on the flexor surfaces of the wrist and on the buttocks, and in a period of five months they spread to the thighs, legs, arms and forearms almost solidly, with scattered areas of papules on the trunk and in the scalp. These became thickened, scaly and at times moist. Treatment overseas consisted of injections of a bismuth preparation and an arsenical, with solution of potassium arsenite administered by mouth. While he was en route to the United States, and after his arrival here the hypertrophic areas improved rapidly without further treatment. He lost no weight and considered his diet adequate.

On examination the skin was rough and dry over the areas formerly affected. Many darkly pigmented atrophic scars remained over these areas. In the scalp they persisted as scars in which there was no hair. On the forearms and ankles several hypertrophic actively pruritic areas were present. These were either nodules or large elevated plaques, up to 5 cm in diameter, with a dry horny surface. The palms, soles and oral mucosa were not involved. There were no signs of vitamin deficiency.

Biopsy from a lesion on the forearm which appeared clinically active showed moderate hyperkeratosis, most evident near the outlets of the oil glands. There was moderate acanthosis. The rete pegs were shortened, and the basal layer of cells was absent or indistinct. The upper portion of the cutis was composed of young connective tissue. This contained a sharply demarcated layer of infiltrate, composed predominantly of lymphocytes but with neutrophils and plasma cells present.

CASE 2—M V, a white man aged 27, had been in the tropics for two months and had gone directly to New Guinea from the United States. In that time he had taken one tablet (0.1 Gm.) of quinacrine hydrochloride

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daily. He had lost 15 pounds (6.8 Kg) in weight and had considered his diet poor in quantity and quality.

The eruption first appeared on the ankles and the dorsa of the hands. Within a few weeks it spread over almost the entire body. Areas unaffected by papules and nodules were erythematous, and the itching was intense. He was given three injections of a bismuth preparation and treated with local applications, without benefit. On the return trip to the United States the lesions began to clear rapidly.

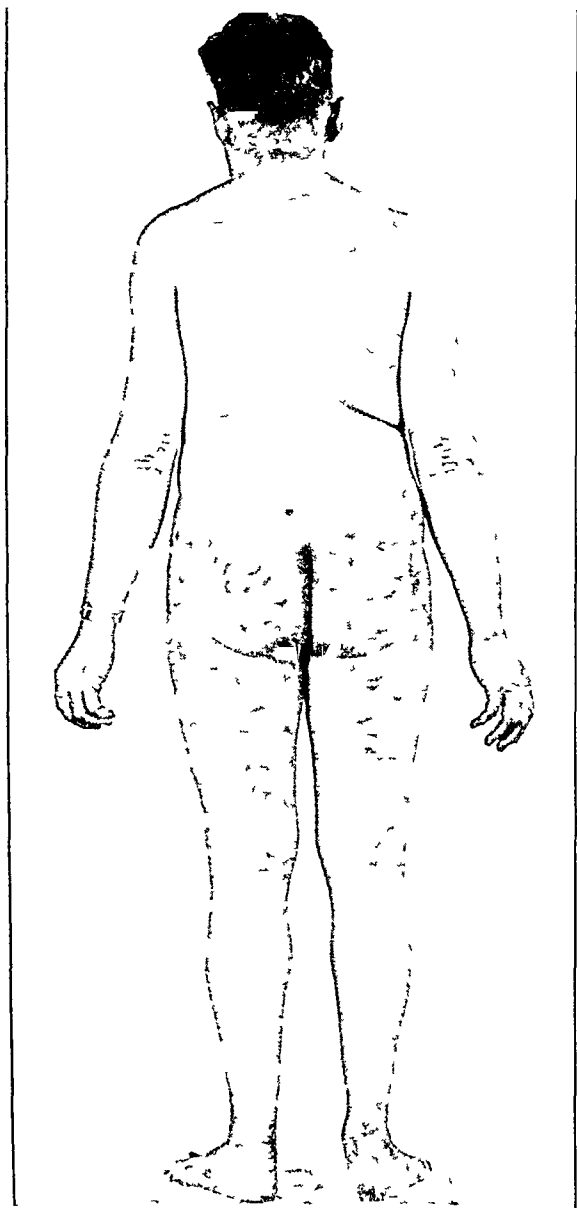


Fig 1 (case 1) —Generalized lichen planus-like eruption, sparing the trunk.

On examination the patient presented numerous purplish to dark brown macules scattered over the entire body, including the scalp, palms and soles. Leukoplakia-like patches were found on the dorsum of the tongue. The remainder of the oral mucosa was free of eruption. Active hypertrophic nodules and plaques remained on the forearms, on the dorsa of the hands and on the ankles. There were fissures at the angles of the mouth but no other signs or symptoms of avitaminosis.

Biopsy from a lesion on the forearm showed moderate hyperkeratosis. The epithelium was decidedly atrophic,

with complete disappearance of the rete pegs. Loose connective tissue composed the papillary and subpapillary layers, and this was diffusely infiltrated with lymphocytes and plasma cells. The lower border of the infiltrate was sharply demarcated. Many cells contained phagocytosed pigment.

CASE 3—M C O, a 42 year old white man, had been in the tropics for fifteen months prior to the onset of his disease. He was at first stationed in the New Hebrides and in New Guinea, but he had been in the Admiralty Islands six weeks when the eruption began. For the previous six to eight months he had taken one quinacrine hydrochloride tablet daily. He had lost no weight and had considered his diet adequate. The eruption first appeared on the wrists and ankles, and in a few weeks it had spread generally, accompanied with severe itching. He received local medication only and improved rapidly on the way home.

On examination there were fissures at the angles of the mouth but no other signs of vitamin deficiency. Deeply pigmented atrophic scars were dispersed over the cutaneous surface except on the face, scalp and soles. The back, abdomen and chest showed fewest lesions. The oral mucosa was normal. The arms, forearms, thighs and legs showed almost complete involvement. On the forearms, legs and ankles there remained active raised lesions covered with a rough horny surface. These were up to 3 cm in diameter.

Biopsy from a lesion on the forearm showed some hyperkeratosis. There were thinning of the granular layer and partial atrophy of the rete pegs. The basal cell layer had disappeared. The upper portion of the cutis was composed of vascular granulation tissue. In this area, sharply limited at its lower border, there was a moderate infiltrate of lymphocytes, plasma cells and neutrophils. Some of the macrophages contained phagocytized pigment granules.

CASE 4—T J M, a white man aged 44, spent three months in New Guinea and then was transferred to the Admiralty Islands, where one month later the eruption began. He had taken 1 quinacrine hydrochloride tablet daily. During this time he had lost 25 pounds (11.3 Kg) in weight and considered the quality of his diet poor.

His eruption appeared first on the calves as a pustular eruption which soon spread to the remainder of the body. As the pustules dried, they were replaced by thickened red to purplish papules and nodules, which itched moderately.

Treatment consisted in the use of local applications and the ingestion of vitamin capsules of unknown content. En route to the United States and afterward most of the eruption improved rapidly, leaving pigmented areas, and the itching ceased.

On examination there were no changes indicating a vitamin deficiency. He presented thinned pigmented areas up to 2 cm in diameter, most noticeable over the upper part of the back, the chest and the buttocks. Involvement of the face and eyelids was slight. Active confluent hypertrophic nodules and plaques, of a dark red color with a white to grayish scale, were present on the forearms and arms, on the dorsa of the feet and on the dorsal and palmar surfaces of the hands. On these areas there were also scattered, small, discrete and confluent flat-topped papules, angular in outline and red to purplish in color, with central umbilication and white striae. The lesions were typical of lichen planus. The tongue and oral mucosa showed numerous areas characteristic of lichen planus in that region.

Biopsy of a section from a regressing lesion on the forearm showed hyperkeratosis. The granular layer

was decidedly thinned. Atrophy of the rete pegs and liquefaction degeneration of the basal cell layer were noted. The papillary and subpapillary layers were represented by vascular granulation tissue. These layers contained focal collections of lymphocytes and some plasma cells. Similar collections were found deeper in the cutis.

CASE 5—W. C., a white man aged 47, had been in the tropics nineteen months when the eruption started. Most of this time he had been in the New Hebrides. He had then spent one day ashore in New Guinea and

On examination there were no abnormalities except those of the skin. Pigmented macules were scattered over the face, including the eyelids, and on the chest, hands, buttocks, legs and soles. Most of the areas faded in color and cleared completely during two months of observation.

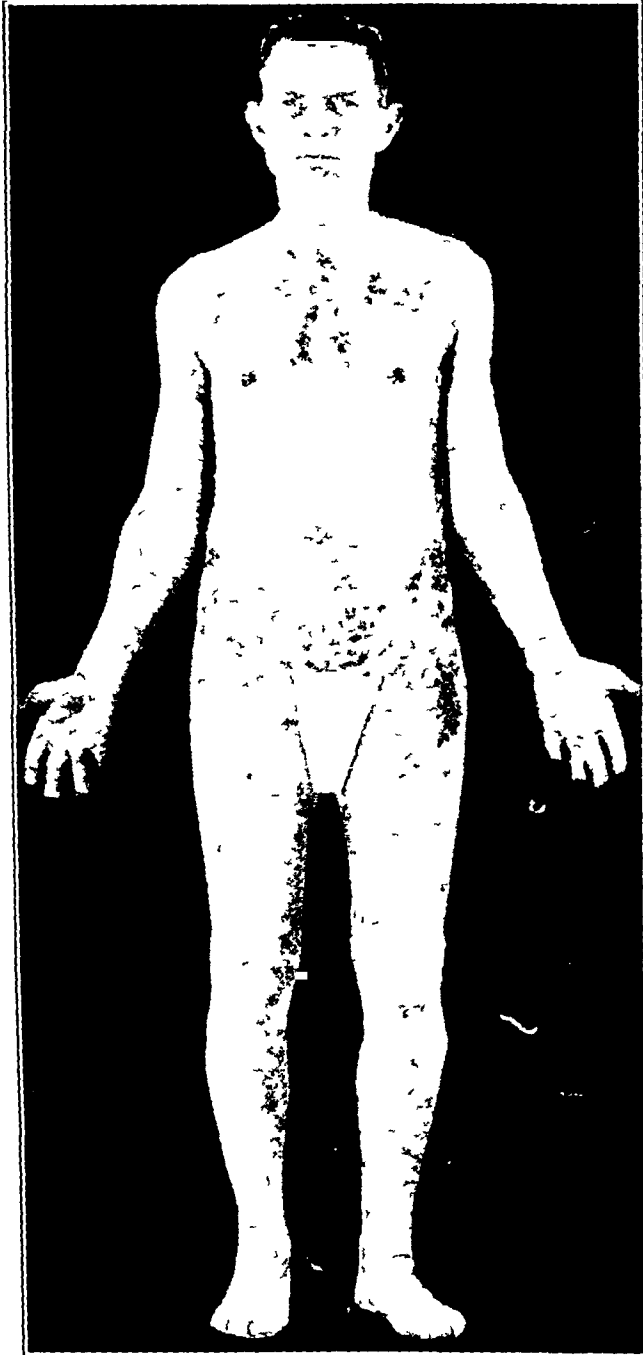


Fig 2 (case 4)—Generalized lichen planus-like eruption (in places, of hypertrophic type) sparing the mid-trunk

had last been in the Admiralty Islands for five and a half months. He had taken 1 quinaquine hydrochloride tablet daily and had lost no weight. Several months previously he had had an attack of dengue. The eruption began on the hands and fingers and then spread generally. At first it appeared as typical papules of lichen planus, later becoming thickened, and confluent and forming a grayish dry scale. There was only slight itching. It began to clear on the patient's return to the United States.



Fig 3 (case 4)—Diffuse scaly patches on the fore-arms



Fig 4 (case 4)—Hypertrophic lesions on the legs

Biopsy of a specimen from a slightly thickened plaque on the forearm showed moderate hyperkeratosis with plugging of hair follicles. There was acanthosis in some areas but thinning of the granular layer in others.



Atrophy of the rete pegs and partial disappearance of the basal cell layer was noted. The papillary and sub-papillary layers were represented by young connective tissue containing a cellular infiltrate which was sharply

All 5 men were in good mental and physical condition at the time of examination. Roentgenograms of their chests were normal.



Fig 5 (case 3) —The histologic structure of lichen planus is satisfactorily shown, although the lymphocytic infiltration in the corium is scanty.



Fig 6 (case 4) —The histologic structure is compatible with that of lichen planus, though the corium is rather scanty.

delineated at the lower border. This was composed principally of lymphocytes and plasma cells. A few neutrophils were present. There was much phagocytosed pigment in the macrophages.

except for T. J. M. (case 4), who showed evidence of a calcified Ghon tubercle and effects of previous inflammation of the base of the right

aura The sedimentation rate was high only in I C O (case 3), who had a rate of 17 mm per hour The Kahn reaction was negative, and the urine was normal on repeated examinations or all the men Complete blood counts revealed no abnormalities of the red or white cells, in the hemoglobin or in the differential percentages

Dr Hamilton Montgomery, of the Mayo Clinic, examined the sections He stated that 'they were consistent with what has tentatively been labeled 'New Guinea lichen planus'' He had examined numerous histologic sections from persons with the same disease from other sources and was of the opinion that it is a new clinical entity, in that features of eczematoid dermatitis or exfoliative dermatitis are mixed with those of lichen planus, while in ordinary lichen planus one never sees "eczema" associated with the process

Dr Zola Cooper, of the Barnard Free Skin and Cancer Hospital, St Louis, thought that the sections fitted the microscopic picture of lichen planus She stated that "all the slides show the hyperkeratosis, the acanthosis with distortion or flattening of the rete pegs, which is characteristic of lichen planus Four of the 5 patients showed some liquefaction degeneration of the basal layer In all of them there was a lymphocytic infiltrate in the upper third of the dermis and an increase in chromatophores in this region There was dilatation of blood vessels in the papillary portions of the dermis"

#### COMMENT

All the affected personnel coming to my attention have been shore-based The greater number of cases have developed in the New Guinea area, but 2 patients of my series had not been in New Guinea, and 1 patient had spent only one day ashore on the island

Most of these men had lost weight before the eruption began A few showed signs, or questionable signs, of vitamin deficiency Loss of weight and distaste for the rations provided are, however, complaints common to nearly all troops in the tropics

Although 4 of the 5 patients were in their forties, the disease has been observed in a number of men in the third and fourth decades The

youngest patient seen was 18 years old I have seen no Negroes with this disease

Nearly all had received treatment Local applications, solution of potassium arsenite injections of a bismuth preparation and oxophenarsine hydrochloride were used singly or in combination on various members of the group with possible benefit in some Nearly all showed improvement en route to the United States and after their return

Dietary deficiency and toxicity of or sensitivity to quinacrine hydrochloride have been suggested as possible causes of these eruptions I feel that additional factors are involved, for the following reasons

1 Several men with lichen planus were seen in the eastern part of the Solomon Islands in 1943 but none with this atypical form was observed Many more cases of this eruption have appeared in 1944 than in 1943, though the administration of quinacrine hydrochloride and the dietary allotments were the same for both years

2 Various forms of lichen planus had been observed long before quinacrine hydrochloride came into use

3 I have administered quinacrine hydrochloride to 5 men nearly well of this disease, giving each three tablets daily for four days, (admittedly a short trial) without causing a flareup of their lesions

4 The eruption has none of the features usually associated with dietary deficiencies or with drug eruptions

5 The disease has appeared in men who had been in the tropics for only two or three months, in which period it is not likely that severe avitaminosis would occur

#### SUMMARY

Numerous cases of a disease which clinically and histologically resembles lichen planus have appeared recently in the tropical islands of the Pacific Ocean In nearly all cases there is a striking similarity in severity and in widespread involvement of the skin It is doubted that toxicity of or sensitivity to quinacrine hydrochloride or dietary deficiencies are the only causes, and it is believed that further investigation will show that some unusual combination of factors is necessary to produce this disease

# ARMY AIR FORCES DERMATOLOGY PROGRAM

LIEUTENANT COLONEL J R SCHOLTZ

MEDICAL CORPS, ARMY OF THE UNITED STATES

Through the foresight and vision of Major General David N W Grant, the Air Surgeon, and of Colonel William P Holbrook, Chief, Professional Division, Office of the Air Surgeon, a dermatology and syphilology branch was established in the Office of the Air Surgeon, Headquarters, Army Air Forces, in August 1944. It was recognized that diseases of the skin represent an important problem in medical care, as indicated by the case load, both in outpatient dispensary care and in Army hospitals, causing disability and time lost from duty. It was further recognized that as American armed forces began operating in increasing numbers in overseas theaters, particularly in the areas of the Pacific and the Orient, cutaneous diseases would become increasingly prevalent and of increasing importance, both from medical and from military standpoints.

Examination of available data revealed that for the entire Army in the continental United States during the year 1943, the over-all admission rate due to cutaneous diseases was 39.6 per thousand. This included only persons actually admitted to hospitals or quarters, in other words, patients disabled and off duty because of skin diseases. The average time lost per patient admitted was thirteen days. Seventy-two and five-tenths per cent of all admissions for cutaneous diseases were accounted for by the following conditions: (a) pyogenic infections, including cellulitis, (b) superficial mycoses, (c) dermatitis venenata, (d) scabies, (e) acne vulgaris, (f) verruca vulgaris, (g) miliaria and (h) various unclassified dermatitides.

It is variously estimated that the number of persons with cutaneous diseases who are treated while on duty is from two to three times that of those admitted to hospitals or quarters.

## FUNCTIONS OF THE DERMATOLOGY AND SYPHILOLOGY BRANCH

The functions of the dermatology and syphilology branch, Office of the Air Surgeon, are as follows:

- 1 Establishment of dermatologic services in A A F regional hospitals,

Headquarters Army Air Forces, Office of the Air Surgeon, Washington, D C

- 2 Development of dermatologic consultation services for A A F station hospitals,
- 3 Achievement of optimum use of specialist personnel now with the A A F,
- 4 Formation of a consultative and preventive program for civilian employees of the Air Technical Service Command,
- 5 Development of a teaching program for residents and general service medical officers,
- 6 Accumulation and analysis of data concerning morbidity, time lost from duty through hospitalization and "sick call load" due to cutaneous diseases,
- 7 Reduction of morbidity, time lost from duty and "sick call load" through improved professional care and administrative practices,
- 8 Coordination and development of clinical studies in those cutaneous diseases which are of particular significance in A A F personnel by virtue of the type of duty or the geographic location,
- 9 Establishment and maintenance of progressive treatment practices in the clinical management of syphilis and other venereal diseases occurring among the military personnel of the A A F,
- 10 Inspection of A A F hospitals and medical installations and evaluation of the quality of the dermatologic service.

## PERSONNEL

At the time the branch was created there were twenty-two medical officers classified as dermatologists in the A A F in the continental United States. Sixteen of these were certified by the American Board of Dermatology and Syphilology. Others, although not certified, had received sound training in recognized dermatologic centers and had had several years in civilian practice limited to dermatology and syphilology. Some of these men were already established in a dermatologic service in an A A F hospital, but others were not. At the time of writing a total of thirty-two medical officers have been classified as dermatologists in the A A F in the continental United States. Twenty-two of these men are now certified by the American Board of Dermatology and Syphilology.

## FUNCTIONS OF A A F DERMATOLOGISTS

A A F dermatologists now perform the following duties. Each has developed a dermatologic service in the A A F regional hospital in which he is stationed. This service includes a ward for the hospitalization of patients with severe, disabling dermatoses and for the definitive treatment

of patients who may be referred from satellite hospitals at which specialized medical care is not available. In addition, each dermatologist conducts clinics for outpatients treated on duty, such clinics being held several times a week or more, depending on the case load.

A A F hospitals in the continental United States are now of two classes: the regional hospitals which are completely staffed with qualified men in all branches of medicine and surgery and which are designed to supply definitive medical care of all types and to serve as consultation hospitals for a given geographic area and, second, the station hospitals, which are staffed to care for common, uncomplicated diseases and to provide emergency care at the station in which they are situated. The station hospital is limited as regards its specialist staff, and, as now organized, no provision is made for a dermatologist on the staff. Thus, all patients who require a specialist's care are referred to a regional hospital, or a specialist is requested to visit the station hospital. The A A F has recently established a consultation system whereby at least one professional consultant from the regional hospital will visit each satellite station hospital each month. There are now thirty regional hospitals, each one of which serves as a consultation hospital to a number of station hospitals in the general area. A A F dermatologists are participating in the consultation system now established.

A number of dermatologists selected by the Office of the Air Surgeon are carrying on a preceptor type of training for medical officers. The purpose of this training is to indoctrinate medical officers (who are not dermatologists) in the management and treatment of the common cutaneous diseases which are observed in the military service. The training lasts three months, the trainee being assigned to the dermatologic service of a dermatologist certified by the American Board of Dermatology and Syphilology who has had association with a civilian teaching institution. The trainee assists in the management of the ward and the outpatient clinics and visits civilian teaching institutions in the vicinity when these are available. This type of training was established because of the extremely limited number of qualified dermatologists in the air forces and because of the need for large numbers of men who could satisfactorily manage common cutaneous diseases at A A F stations to which no dermatologist was assigned. At the present rate of training approximately fifty medical officers will receive this type of indoctrination each year, and it is believed that a major contribution will have been made to the conservative management of

cutaneous diseases in the A A F. Some of the men receiving this training may become interested enough to carry their studies further after their return to civilian life and take formal training in dermatology. The training now given in the A A F was not established with the idea that these men would become qualified dermatologists simply by virtue of such training thus received. In the establishment of the program, it was specifically directed that men receiving this training would not be classified as dermatologists on the basis of the training received.

The Air Technical Service Command of the Army Air Forces, which is responsible among other things for the maintenance and repair of aircraft, operates a number of large depots throughout the continental United States in which several hundred thousand civilians are employed. It has been estimated that 35 per cent of these employees are exposed to occupational hazards and to chemical agents which may cause dermatitis. Patients at these depots are served by medical officers trained in industrial medicine, but with few exceptions a trained dermatologist has not been available for consultation. Arrangements have been made for the A A F dermatologists in the general area of these depots to make regular visits to assist in the diagnosis, management and proper classification of cutaneous diseases occurring in the civilian employees. This service has already resulted in more accurate classification of cases and in the evaluation of the role of occupation in the causation of disease. It has also resulted in more prompt return to duty and in shortened periods of disability. It is expected that during the coming years valuable information will be gathered with reference to the occupational hazards of a cutaneous nature encountered in the maintenance and repair of aircraft.

#### A A F MANUAL ON MANAGEMENT OF CUTANEOUS DISEASES

A study of patients hospitalized for cutaneous diseases in the Army revealed that perhaps 50 per cent were hospitalized as a result of improper early treatment. Furthermore, it was found that approximately 90 per cent of all diseases of the skin occurring in the Army fall within a small number of diagnoses. Because of these facts it was considered entirely practical to publish a brief guide in outline form on the management of the common cutaneous diseases seen in the military service, for use by A A F medical officers, the vast majority of whom had received no specific training in dermatology. It was be-

lieved that if this manual was followed in initiating the treatment of persons seen on an outpatient status, the number of patients aggravated by improper and irritating sensitizing treatment and consequently hospitalized, could be greatly reduced. Accordingly, a brief manual in outline form was prepared by a group of five dermatologists of the Army Air Forces and published as A A F Manual 25-1, subject "Management of Common Cutaneous Diseases".<sup>1</sup> It has been distributed to all A A F installations within the continental limits of the United States for use in dispensaries and station hospitals. It is not "directive" in nature, and in no way limits the exercise of clinical judgment on the part of the medical officer.

#### SUMMARY

The dermatology program being developed in the Army Air Forces has progressed along the

1 Management of Common Cutaneous Diseases, Army Air Forces Manual 25-1, United States War Department, Washington, D C, Government Printing Office, October 1944, revised, Dec 22, 1944

following lines. Available specialized personnel have been utilized to the fullest extent by placing them in A A F Regional Hospitals, in which they establish dermatologic services and from which they act as consultants to station hospitals in their geographic areas. Selected dermatologists with previous teaching experience and certified as specialists by the American Board of Dermatology and Syphilology are being used to train a number of internists in the fundamentals of military dermatology. A A F dermatologists are being used as consultants in the industrial medical program of the Air Technical Service Command. A manual on the management of the common cutaneous diseases seen in the military service has been published and distributed to A A F installations in the continental United States. A branch of dermatology and syphilology has been established in the Office of the Air Surgeon, Headquarters, Army Air Forces, to initiate, coordinate and develop the program outlined herein.

# DERMATITIS FROM DEHYDRATION OF POTATOES

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The dehydration of vegetables is a relatively new industry. In the last few years, because of the needs of the armed forces and of lend-lease for a food with a high caloric value which would occupy relatively little shipping space, there has been a great increase in the number of plants which dehydrate potatoes. Most of the dehydrating plants in the state of Idaho have been in existence for two years or less. The majority of the plants are situated in the great potato-raising regions.

In the last two years, more than 200 cases of so-called potato poisoning or dermatitis have been reported to the Idaho Industrial Accident Board. The United States Public Health Service was requested to investigate the cause of the dermatitis among workers processing the potatoes.

We know of no other published reports of dermatitis from potatoes.

## DEHYDRATION PROCESS

Six plants in which the potatoes were dehydrated were investigated. In only one of them was lye used in the peeling process. In this plant, after the potatoes have been washed with water, they are precooked (210 F.), immersed in 10 per cent solution of lye in a lye cooker for five minutes and then peeled by friction in a rotating drum. The washing water in this process finally removes all traces of the lye. In the other five plants, the potatoes are precooked and then peeled by rough rubber rolls. In all cases, no lye was used.

After they have been peeled, the potatoes are placed on moving belts which travel down the centers of long tables. Women workers seated on each side of these trimming tables remove the eyes and the remnants of the peel with special-shaped trimming knives. In this operation, the hands are constantly wet with water and potato juice. In nearly all cases, the derma-

titis reported developed among the workers at the trimming tables.

After the trimming operation, the potatoes are cut into small pieces by machine, blanched by steam to destroy the potato enzyme (tyrosinase) and thus prevent discoloration and finally dehydrated in wind tunnels by exposure to air heated to a temperature of 150 to 155 F. for nine hours. The dehydrated potatoes weigh one eighth of their original weight and contain only 3 per cent of their original water content. The final product has a moisture content of approximately 7 per cent.

The plant in which the lye was used for peeling was the largest one visited and had the greatest number of cases of dermatitis. In this plant, and in others, it was the custom, because of the great press of work, for the workers to be employed for seven consecutive days every other week, on eight hour shifts. In alternate weeks they worked six days. This long period of exposure without intervals of rest was an important contributing factor to the dermatitis.

## CLINICAL INVESTIGATIONS

Twenty-four women with dermatitis were seen. It took from two weeks to one month for enough discomfort from the dermatitis to develop so that workers either reported to the plant physician or stopped working. In all but 3 of the workers, the dermatitis was limited to the hands. These 3 patients had, in addition to dermatitis on the hands, involvement of other parts of the body, such as arms, legs, scalp and face. In these 3 cases the dermatitis was found to be of nonoccupational origin, namely, atopic dermatitis, dermatophytosis and psoriasis, respectively.

The earliest manifestations of dermatitis from the handling of the potatoes were seen on the hand which grasps the potato in the trimming operation. First to be affected was the skin of the web spaces between the fourth and fifth and the third and fourth fingers. The changes consisted of redness, scaling and, in a few instances, vesicles. As the condition progressed,

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the involvement resembled *erosio interdigitalis blastomycetica*. The lesions in many instances were not sharply demarcated and extended up the sides of the fingers. There was, in addition, evidence of maceration of the skin on the rest of the hand, the skin of the palm in most of the workers who did not wear gloves showed varying degrees of maceration, such as whiteness and puckering. In many instances this went on to dryness, redness and scaling of the palms, with the formation of fissures in the folds of the skin, especially at the bases of the terminal phalanges, in the more severely affected workers. Involvement of the skin of the dorsum of the fingers was also observed in some of the patients. In a number of instances, the web spaces of both hands were affected, in others, only the skin of the hand grasping the potato was involved. A combination of palmar and web space lesions was seen only in those patients in whom the dermatitis had existed for some time. In no instances did the dermatitis extend above the wrist, and no changes in the nails were seen.

Since the greatest number of cases were observed in the plant in which lye was used to remove the peel, the question naturally arose as to whether enough alkali remained on the surface of the potato to play a role in the cause of the dermatitis. Tests for any alkali remaining on the surface of the potatoes showed that the natural acidity of the potatoes would neutralize any traces of hydroxide which would remain after peeling. Such sound potatoes had a surface  $p_H$  of 5.7 to 6. Only in defective potatoes with deep cracks due to rot was the water prevented from completely removing the lye. Such potatoes were not many, since previous inspection removed the rotted vegetables before they came to the trimming tables.

Alkalinity was further ruled out as a contributing cause of dermatitis by the fact that in plants in which the lye was not used similar changes in the skin were also observed.

*Patch Tests*—Although it was evident that the dermatitis was due primarily to maceration of the skin from long hours of immersion in water and from contact with the vegetable juice, patch tests were made to rule out the possibility of allergic dermatitis. The patch tests were made with slices of potato, including cooked and uncooked portions, which were applied to the normal skin of the forearm of 12 patients with dermatitis and of 5 controls that is, persons who did not work in the plant. All of the patch tests elicited negative reactions.

*Cultural Studies*—Cultures were made on Sabouraud's medium from the unbroken vesicles

and from the margins of the lesions in the web spaces of 6 of the patients. Cultures (identification made by Dr. Emmons) revealed no significant results, with the exception of the isolation of *Monilia albicans* from 1 patient. *Monilia albicans* is the organism associated with the syndrome *erosio interdigitalis blastomycetica*.

#### COMMENT

It is our conclusion that the dermatitis seen in the processes of dehydrating potatoes is an occupational disease due to the long hours of exposure to water and potato juice which results in varying degrees of maceration of the skin. Secondary invasion by cocci and monilia organisms also play a role in the clinical syndrome.

Proper protection of the skin by ointments and gloves easily prevented the dermatitis. We were able to note this because in a number of the plants visited in which proper protection measures were used almost no dermatitis was seen.

#### RECOMMENDATIONS AND PREVENTION

- 1 All workers handling the potatoes, especially those at the trimming tables should wear rubber gloves. These gloves should be turned and cleaned each day. Employees should also wear impervious sleeves which fasten over the gloves at the wrist. It is advisable that the management furnish one pair of these gloves each month if necessary, because in this way the wearing of gloves can be made compulsory. If at any time the gloves are lost or torn they should be replaced by the management.

- 2 Because there are frequent punctures of the gloves by the trimming knives, the workers should apply an emollient ointment to their hands. Care should be taken that it is applied to the web spaces. Thus, if any punctures should occur, the hands would still be protected by a water-repellent film, while the wearing of the gloves would prevent the ointment from contaminating the potatoes.

- 3 At each rest period, at lunch time and before going home, the workers should be instructed to wash their hands thoroughly in warm water and with a mild soap, or a soap substitute, and to apply the emollient ointment.

- 4 Those workers in whom dermatitis develops should be carefully supervised in their routine of protection and should be given an emollient cream to take home to counteract further the effects of the maceration of the skin. Patients with chronic dermatitis with involvement of the web spaces should be examined for secondary infection with cocci or monilia organisms. If pathogenic organisms are demonstrated proper treatment should be instituted.



# URTICARIA FROM PERFUME

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Scent, whether organic or inorganic in origin, has a physicochemical basis and is propagated by minute particles. These odoriferous particles are termed osmyls and may act as inhalant allergens. The subject of allergy to scent or to osmyls has received but meager attention, if one is to judge from the few brief references in the literature. Among the authors who have advanced this etiologic conception are Feinberg and Aries,<sup>1</sup> Rappaport and Hoffman,<sup>2</sup> Urbach,<sup>3</sup> Sulzberger and Wolf<sup>4</sup> and Horesh.<sup>5</sup>

That perfumes as contactants frequently cause dermatitis is well known. Downing,<sup>6</sup> Schwartz and Tulipan,<sup>7</sup> and Rattner and Pusey,<sup>8</sup> to mention but a few, have repeatedly called attention to the importance of scented cosmetics as a cause of dermatitis. The role of perfume, however, as an allergen causing chronic urticaria due to inhalation of osmyls has been seldom considered.

A report, therefore, of a case of chronic urticaria of six years' duration due to the use of perfumes is deemed worthy of publication.

## REPORT OF A CASE

T. B., a white housewife, aged 45, had been suffering since 1939 from chronic recurrent urticaria. The initial attack consisted of a group of hives on the face, neck, arms and legs. Since that time she had never been

1 Feinberg, M., and Aries, P. L. Asthma from Food Odors, *J A M A* **98** 2280 (June 25) 1932

2 Rappaport, B. Z., and Hoffman, M. M. Urticaria Due to Aliphatic Aldehydes, *J A M A* **116** 2656 (June 14) 1941

3 Urbach, E. Odors (Osmys) as Allergenic Agents, *J Allergy* **13** 387 (May) 1942

4 Sulzberger, M., and Wolf, J. Dermatologic Therapy, Chicago, The Year Book Publishers, Inc., 1940, p. 175

5 Horesh, A. J. (a) Allergy to Odor of White Potato (Irish Potato), *J Allergy* **15** 147 (March) 1944, (b) Allergy to Food Odor. Its Relation to the Management of Infantile Eczema, *ibid* **14** 334 (May) 1943

6 Downing, J. G. Cosmetics Past and Present, *J A M A* **102** 2088 (June 23) 1934

7 Schwartz, L., and Tulipan, L. A Text Book of Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939

8 Rattner, H., and Pusey, W. A. Neurodermatitis or Irritant Dermatitis, *J A M A* **99** 1934 (Dec 3) 1932

free from lesions. At times there were only a few, but at other times the entire cutaneous surface was affected.

During these six years, she was under the care of competent dermatologists, allergists, internists and surgeons. Dermatologic management consisted of injections of histamine or calcium, ingestion of ephedrine and injections of epinephrine hydrochloride. Roentgen ray therapy, ultraviolet irradiation and autohemotherapy were also used to no avail. The allergists made a complete study in their field without any definite results. The internists looked for foci of infection, and both a tonsillectomy and a hemorrhoidectomy were performed in January 1944. After all probable etiologic factors had been considered and ruled out, the patient was told that her hives were due to her neurovascular instability and that she should try to forget about her ailment.

She had had no other allergic symptoms, such as allergic rhinitis, asthma, migraine or dermatitis.

The patient was first seen by one of us (S. J. Z.) on Aug. 15, 1944. After we had listened to her history and had noted that she used much perfume, she volunteered the explanation that the collection and liberal use of perfumes were her hobbies. Not only did she use perfume and scented cosmetics constantly, but a list of the latter revealed forty-eight different perfumed preparations. On every coat hanger, in every garment bag and in every drawer in her dresser, she had sachets.

Routine physical and laboratory examination failed to disclose any pathologic conditions. She was advised to remove all traces of perfume from her clothing, to use unscented cosmetics and to keep away from persons using much scent. She was not given any medication, not even local applications.

On August 23, after one week of living in an atmosphere, free from perfume, her hives disappeared. A week later she reported an attack of hives following a bridge party in a room with forty women who were liberal users of perfume. On September 6, the patient said that she had suffered no further attacks. Later, on September 14, she reported that she was feeling better than she had for years and was free of hives.

On September 21, when the suggestion was made that she use one perfume at a time, in order to find out which one she was sensitive to, the patient refused, saying that she did not wish to suffer the agonies of hives again.

## COMMENT

Consideration of the chemistry of the various materials used in the manufacture of perfumes, toilet waters, scented cosmetics and other toilet preparations will rationalize the diagnostic procedure in this case and will be helpful in the diagnosis in other cases in which perfumes act as contact or inhalant allergens.

A finished perfume consists of a solution of perfume oil in 90 per cent ethyl alcohol, a toilet water or cologne contains less perfume oil in



the same solvent. In recent years, owing to the shortage of ethyl alcohol, so-called cream and solid perfumes have been marketed. They are emulsions of perfume oils with varying amounts of mineral oils and waxes, depending on whether a liquid, a cream or a solid product is desired.

In scenting cosmetics and toilet preparations, the amount of perfume oil is generally determined by the retail selling price of the finished cosmetic. Usually, the more expensive cosmetics contain a larger quantity than the cheaper ones, a fact which undoubtedly explains the more frequent occurrence of allergies to perfume in users of higher-priced cosmetics.

The compounding of a finished perfume oil is an art rather than a science. There remains much to be done in determining the chemistry of the raw materials used. A consideration of these materials will illustrate the complexity of this problem.

As many as thirty different materials are employed to obtain some of the popular odors. Some of these substances are used for their odor values alone, some, for their value as fixatives—then ability to make a perfume fragrant even after the alcohol has evaporated and some, both for odor and as fixatives.

Raw materials used in perfumes may be divided into two groups based on their origin: (1) vegetable, (2) animal and (3) synthetic. Those of vegetable origin are used in the form of volatile oils (essential oils), balsams or resins. Those of animal and of synthetic origin are complex chemical substances apparently formed by oxidation and polymerization of volatile oils.<sup>9</sup> They are less important in perfumery than are the essential oils, and comparatively little is known of their chemical structure.

The essential oils are derived from flowers, fruits or their seeds, roots of plants and even the wood of some trees. As used by the perfume industry, they are only partially purified. In many instances, then, it is not known whether the allergic reactions caused by certain commercial essential oils are due to the basic oil or to some impurity.

Many essential oils have been partially analyzed. Some knowledge, therefore, of the structure of the compounds found in them is available. Alcohols and phenols have been identified. Aldehydes and ketones are found, as are also ethers and esters. Many also contain terpenes.<sup>10</sup>

Since many components of the various natural oils have been identified and their chemical structures determined, it has been possible to duplicate them in the laboratory. Many natural flower and fruit odors are being approximated by the use of synthetic chemicals.

The search for new synthetic compounds to take the place of the natural odors which have thus far defied duplication has been a more or less hit-and-miss affair. It has been noted by chemists specializing in this field that there is a certain resemblance between chemical structure and odor, but there has been no definite relationship established between chemical constitution and odor.<sup>11</sup> The chromophore, or "color bearer," theory of dyes has inspired some work in this field, but only a start has been made. It is hoped that eventually a definite relationship will be established.

There seems to be a relationship between the chemical structure of natural and of synthetic essential oils and their allergenic properties, but here, too, there is much to be done. Thus far, it can be said that the unsaturated compounds, such as certain aldehydes and ketones, seem to be more irritating and allergenic than saturated compounds, in which the carbon linkages are satisfied. For instance, the citrus oils, known to be the worst offenders, all contain citral, an aldehyde with two unsatisfied olefinic carbon linkages.<sup>12</sup>

Only four substances of animal origin—ambergris, castor, musk and civet—are employed in perfumery. Their chemical structure is generally unknown. They are used primarily for their value as fixatives.<sup>9</sup>

Many natural and synthetic essential oils are used as fixatives. The one most liable to cause trouble is oil or oleoresin of orris. At one time the root of the iris (orris) was dried, powdered and used in cosmetic powders, sachets, dry shampoos and the like. Since it has been generally recognized that orris root powder frequently causes allergic reactions, the use of powdered orris root has been almost completely discontinued by cosmetic manufacturers. Unfortunately, the oil and the resin continue to find wide use as fixatives in perfumes.

Most cosmetic manufacturers do not compound their own perfume oils. These are purchased from firms which import and compound the various raw materials. The cosmetic or

<sup>9</sup> Askinson, G. W. *Perfumes and Cosmetics—Their Preparation and Manufacture*, New York, Norman W. Henley Publishing Company, 1922.

<sup>10</sup> Poucher, W. A. *Perfumes, Cosmetics and Soaps*, New York, D. Van Nostrand Company, Inc., 1942, vol. 2.

<sup>11</sup> Moncrieff, R. W. *Chemical Constitution and Odour, Manufacturing Chemist* **14** 33 (Feb.), 60 (March), 95 (April), 130 (May), 174 (June), 205 (July), 239 (Aug.) 1943.

<sup>12</sup> Cheronis, N. F. *Organic Chemistry*, New York, Thomas Y. Crowell Company, 1941.

perfume manufacturer, in most cases, knows nothing of the natural or synthetic oils used. Even if such firms conscientiously omit known allergens or irritants from the cosmetics themselves, they may unwittingly add to their products as perfumes essential oils and synthetic chemicals which are even more allergenic than the starches, gums and other chemicals omitted.

Dealers in perfume compounds will not divulge the composition of the finished products. They generally give each one a number or trade name to avoid duplication. This custom has existed in the perfume industry for years and is accepted by the manufacturers of cosmetics because many cannot profitably employ an experienced perfumer. Furthermore, it is generally believed that the incidence of allergic reactions is too small to interfere with the indiscriminate use of their products.

In view of the complex and partially unknown chemistry of perfume,<sup>10</sup> it must be understood

that to perform patch tests would be complicated, incomplete and unsatisfactory at best.

In the case under consideration and in all cases of allergy in which perfume is suspected to be the etiologic factor, its complete elimination and the use of unscented cosmetics will be quickly diagnostic. When perfume is definitely the cause of the allergy, such elimination of all perfumes and scented cosmetics will likewise be therapeutic.

#### SUMMARY

A case of chronic urticaria, apparently due to the scent of perfumes, was observed. Since the patient refused to submit to laboratory studies, the evidence that the use of perfumes was the etiologic factor is only clinical. Nevertheless, we believe that in studies of allergic diseases perfume must always be considered as such a causative agent not only as a contactant but as an inhalant.

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# PENICILLIN IN THE TREATMENT OF CUTANEOUS DISEASE

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Not since therapy with the sulfonamide compounds was introduced has there been any therapeutic agent as completely studied as penicillin. The startling and almost miraculous results obtained by the use of this agent in the treatment of gonorrhea, meningitis, syphilis and septicemia are well known. It is our purpose to review the results obtained in the treatment of some cutaneous diseases with penicillin locally and parenterally administered.

TABLE 1—*Classification of Forty-One Patients According to Type of Cutaneous Infection*

| Disease   | No. of Patients |
|---|-----------------|
| Sycosis vulgaris                                | 7               |
| Acne (pustular)                                 | 5               |
| Psoriasis                                       | 6               |
| Favus   | 1               |
| Lichen planus                                   | 2               |
| Lupus erythematosus (chronic discoid)           | 2               |
| Impetigo contagiosa                             | 8               |
| Dermatitis seborrheica with secondary infection | 4               |
| Ecthyma   | 1               |
| Pemphigus vulgaris                              | 1               |
| Ludwig's angina                                 | 1               |
| Gonorrheal conjunctivitis                       | 1               |
| Trichophytosis, secondarily infected            | 2               |
| Total   | 41              |

The penicillin obtained was the dry, amorphous, yellowish form, and its sodium salt was the preparation used clinically. The solution employed contained 400 to 600 Oxford units per cubic centimeter. This was applied to the affected areas as a wet dressing, so that the lesions were constantly dampened with the penicillin solution. To prevent the solution from evaporating rapidly, the saturated gauze was well covered with oil-cloth. For the intramuscular injections, 20,000 units of penicillin was mixed with 2 cc of isotonic solution of sodium chloride.

Forty-one patients with varying cutaneous infections were used as subjects for therapeutic trial. Table 1 shows the distribution of diseases represented.

From table 1 it can be seen that there are several disease entities. In attempting to treat these various cutaneous diseases, we were aware

of the methods and observations of Florey and Florey, Roxburgh, Christie and Roxburgh, Johnson and Schoch.<sup>1</sup>

Our intention was to determine the effectiveness of penicillin used locally and parenterally in the treatment of diseases caused by pyogenic organisms and also of chronic, recalcitrant and intractable diseases, such as psoriasis, lichen planus and lupus erythematosus. As far as could be determined, no reports have been rendered on results for these chronic diseases. Our patients were treated empirically.

Table 2 shows that 18 patients were treated by local medication. In all these patients it was possible to identify an organism which by biologic assay should respond to penicillin. The treatment consisted in the use of wet dressings or ointment of penicillin in concentrations of 400 to 600 units per cubic centimeter. In 4 patients with sycosis vulgaris, who previously had been treated with roentgen rays, vaccines and ointments, the response was good and almost immediate. In these 4 persons recurrences were checked by the continued use of penicillin ointment. For 1 patient whose disease was of several years' duration, local treatment was of no avail.

In the persons with pustular cystic acne from which *Staphylococcus aureus* was cultured, little improvement resulted from the use of penicillin in an oycholesterol-petrolatum ointment base.<sup>2</sup> This preparation was applied twice daily for two months. No permanent improvement resulted. The use of penicillin locally for this type of acne was of no avail.

Local treatment was used with dramatic results, for 8 patients with impetigo contagiosa. The pa-

1 Florey, M. E., and Florey, H. W. General and Local Administration of Penicillin, *Lancet* **1** 387 (March 27) 1943. Roxburgh, I. A., Christie, R. V., and Roxburgh, A. C. Penicillin in Treatment of Certain Diseases of the Skin, *Brit. M. J.* **1** 524 (April 15) 1944. Johnson, H. M. Penicillin Therapy of Impetigo Contagiosa and Allied Diseases, *Arch. Dermat. & Syph.* **50** 1 (July) 1944. Schoch, A. G. Local Penicillin Therapy, *ibid.* **50** 202 (Sept.) 1944.

2 The preparation used was aquaphor (Duke Laboratories, Inc.).

tients were treated with wet dressings and penicillin ointment. From their lesions *Staph aureus* and *Streptococcus pyogenes* were recovered. Penicillin assay indicated that these organisms would respond promptly to such therapy. In all the patients there was response within an average of five days.

To 1 patient with recurrent pyogenic ulcers of the leg from which *Staph aureus* and beta hemolytic streptococci were recovered, wet dressings of penicillin gave only temporary superficial improvement. Once crusts began to form, peni-

every three hours for a total of twenty-five injections. The other patient received 1,805,000 units of penicillin intramuscularly and intravenously. The detailed report of the case of the latter patient follows.

A soldier aged 38 stated that in March 1942 he noticed an eruption about the nostrils. He was treated by a civilian physician and cured. Shortly afterward, however, numerous papular and pustular lesions at the corners of the mouth developed. They became more numerous and extended to the face, scalp and axillas. These lesions exuded a clear yellow fluid and then became crusted. After induction into the military ser-

TABLE 2—Local Treatment

| Disease                   | Cases | Average Duration    | Culture   | Penicillin Assay                      | Treatment               | Result                  |
|---------------------------|-------|---------------------|---|---------------------------------------|-------------------------|-------------------------|
| Sycosis vulgaris          | 5     | 7 years             | 4 cases <i>Staph aureus</i><br>1 case <i>Str pyogenes</i> | 3 to 4 cm zone of complete inhibition | Wet dressings, ointment | Cured 4<br>Unimproved 1 |
| Acne (pustular)           | 3     | 5 years             | <i>Staph aureus</i>                                       | 3 to 4 cm                             | Wet dressings, ointment | Unimproved 3            |
| Impetigo contagiosa       | 8     | 6 days              | <i>Staph aureus</i><br><i>Str pyogenes</i>                | 4 cm zone of complete inhibition      | Wet dressings, ointment | Cured 8                 |
| Pyoderma (recurrent)      | 1     | 7 years (recurrent) | <i>Staph aureus</i> and hemolytic streptococcus           |                                       | Wet dressings           | Unimproved              |
| Gonorrheal conjunctivitis | 1     | 11 days             | <i>Neisseria gonorrhoeae</i>                              |                                       | Wet dressings           | Cured                   |

TABLE 3—Parenteral Treatment

| Disease                                    | Cases | Average Duration | Culture  | Penicillin Assay | Treatment                     | Result   |
|--|-------|------------------|--|------------------|-------------------------------|--|
| Sycosis vulgaris                           | 2     | 8 years          | 2 <i>Staphylococcus aureus</i>                             | 5 cm             | Intramuscular and intravenous | Unimproved, 2  |
| Acne (pustular)                            | 2     | 6 years          | 2 <i>Staphylococcus pyogenes</i>                           | 3 cm             | Intramuscular                 | Improved, 2  |
| Psoriasis vulgaris                         | 6     | 12 years         |  |                  | Intramuscular                 | Unimproved   |
| Lichen planus                              | 2     | 2 years          |  |                  | Intramuscular                 | Unimproved   |
| Favus                                      | 1     | 18 years         | <i>Trichophyton crateriforme</i>                           |                  | Intramuscular                 | Unimproved   |
| Lupus erythematosus                        | 2     | 3 years          |  |                  | Intramuscular                 | Unimproved, 2  |
| Seborrheic eczema with secondary infection | 4     | 3 years          | <i>Staphylococcus pyogenes</i>                             |                  | Intramuscular                 | Infection cleared, seborrheic dermatitis, unimproved |
| Pemphigus vulgaris                         | 1     | 6 weeks          |  |                  | Intramuscular                 | Unimproved   |
| Ludwig's angina                            | 1     |                  |  |                  | Intravenous                   | Cured  |
| Trichophytosis with secondary infection    | 2     | ½ year           | <i>Trichophyton gypsum</i><br><i>Staphylococcus aureus</i> |                  | Intramuscular                 | Pyogenic infection and fungous infection, unimproved |

cillin failed, and the lesions would again completely break down. The patient in this case was treated later with injections of oxygen with considerable improvement. (Suggested by Lieutenant De Aguilar.)

Twenty-three patients were treated with penicillin, administered either intramuscularly or intravenously, as shown in table 3. From the table it can be seen that it was impossible to perform laboratory examinations, such as cultures or penicillin assays, in some cases. In this group there were 2 patients with sycosis vulgaris. One received 1,000,000 units of penicillin intramuscularly. He received 40,000 units

in June 1942, the patient received treatment at each station to which he was assigned. This consisted at one time or another of applications of ammoniated mercury, gentian violet medicinal, sulfur ointment, silver nitrate and salicylic acid. He was also given roentgen therapy, a total of 750, and sulfonamide compounds. He made no improvement, and since his condition was incompatible with military duty it was felt that a trial with penicillin in an effort to return him to duty was indicated. Cultures were obtained from the lesions. The offending organism was *Staph aureus*, which when assayed with penicillin was shown to be susceptible to the drug. He was then given an initial dose of 30,000 units of penicillin by intravenous injection, which was followed by 25,000 units intramuscularly every three hours for nine days. He received a total of 1,805,000 units. This was supplemented by local application of penicillin solution (250 and 500 units

per cubic centimeter) twice daily to the lesions. It was sprayed on at first but was later applied in the form of continuous dressings. Treatment was discontinued when it was felt that maximum benefit had been obtained.

This patient while under treatment with penicillin made definite improvement. The axillas were not treated locally and were used as a control. The response in the axillas was as good as that on areas to which penicillin was applied locally. The eruption on the face almost completely cleared and the itching considerably lessened while under treatment. The scalp was the most resistant and made the least improvement, despite frequent shaving and removal of crusts. Unfortunately, the improvement was only temporary, since three days after use of penicillin was discontinued the face and axillas were about in the same condition as prior to treatment.

Results in this case of a chronic, recurrent eruption shows that penicillin is of no permanent value in the treatment of sycosis vulgaris. One also can conclude that although sycosis vulgaris is caused by pyogenic organisms which should respond to penicillin therapy clinically they do not always do so.

In 2 cases of pustular acne, intramuscular injection of penicillin was tried, each patient receiving 1,000,000 units of penicillin. Temporary improvement was noted in both patients about ten days after treatment. The pustules disappeared, leaving fresh scars. Discontinuance of this therapy was followed by a recrudescence of the pustular lesions. Observation of these 2 patients indicates that pustular acne will improve to only a slight degree and this improvement is only temporary.

Penicillin was also used intramuscularly in the treatment of six patients with psoriasis of long standing. These patients gave the usual history of being treated by many dermatologists and with various forms of therapy. Intramuscular injections of penicillin in doses of 1,000,000 units failed to affect the course of this disease in any way. Results in these 6 cases indicate to us that psoriasis still remains a chronic intractable disease.

In 2 cases of chronic lichen planus, in which the same method was used, the results were negligible.

In a case of favus due to *Trichophyton crateriforme* of eighteen years' duration, 1,000,000 units of penicillin, given intramuscularly, failed completely to alter the course of the disease.

As shown in table 3, 2 patients with lupus erythematosus were also treated with penicillin. In 1 the eruption remained unchanged. In the other the course was unchecked and the disease became much worse, as shown by the increase in the sedimentation rate and the dissemination of lesions.

In a group of 6 cases, consisting of 4 cases of seborrheic dermatitis and 2 of fungous infection, in which the patients were obviously secondarily infected, great improvement resulted from therapy with penicillin. Penicillin was also employed in 1 case of pemphigus foliaceus of six weeks' duration. The patient received a total dose of 1,000,000 units intramuscularly but died shortly afterward.

One patient with acute phlegmonous angina, which is usually fatal, responded dramatically to 2,000,000 units of penicillin given by continuous intravenous drip.

No serious toxic reactions were encountered after the clinical administration of penicillin in our patients. Only minor local discomfort was noted after repeated injections. A slight transient fever occurred in 1 (with pyoderma) shortly after intramuscular administration. No cutaneous or gastrointestinal disturbances were observed in this series.

#### SUMMARY

Forty-one patients with cutaneous diseases were given local and parenteral treatment with penicillin. This drug was found to be useful in the treatment of sycosis vulgaris, impetigo contagiosa and gonorrheal conjunctivitis when used locally. Whether penicillin was used intramuscularly or intravenously, it proved to be beneficial for sycosis vulgaris, pustular acne, Ludwig's angina and chronic cutaneous diseases complicated by secondary infection with pyogenic organisms. In our opinion, penicillin therapy is of no value for psoriasis vulgaris, lichen planus, favus, lupus erythematosus, pemphigus foliaceus, and seborrheic and chronic fungous dermatitis.

NOTE—After the submission of this article, patients with cutaneous actinomycosis and leishmaniasis have been treated with penicillin. No permanent beneficial results were obtained. As to reactions to penicillin, urticarial and pityriasis-rosea-like eruptions have been encountered. In 1 patient bilateral hydroarthrosis of both knees occurred.

# IS PENICILLIN A PHOTSENSITIZING AGENT?

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It is a well known fact that penicillin therapy produces few reactions. Urticaria seems to be the most common cutaneous reaction. In this report the possibility is suggested that penicillin acts as a photosensitizing agent.

Photodermatitis of vegetable origin has already been well studied<sup>1</sup>. It is due in most instances to external contact of the patient with the plant followed by his exposure to sunlight. The action of chlorophyll seems to be an important factor in the photosensitizing properties of certain plants. The mechanism of photosensitization by a fungus is undoubtedly different, since fungi lack chlorophyll.

## REPORT OF A CASE

A 25 year old white pilot was admitted to the hospital on Jan 29, 1944 for penicillin therapy. He had had gonorrhea for three weeks. He had received one course of treatment with sulfathiazole from January 5 to January 11 and another, with sulfadiazine, from January 14 to January 19. The total amount administered in the first course was 34 Gm and in the second 37 Gm. The urethral discharge failed to respond to therapy, and the patient was referred to the hospital for treatment with penicillin.

On January 28 the results of laboratory examinations were as follows. A smear of the urethral discharge showed intracellular and extracellular diplococci. A culture from the urethral discharge was positive for gonococci. Urinalysis showed 20 to 25 leukocytes per high power field. The hemogram was normal, and the Kahn reaction of the blood was negative. The results of tests for sulfonamide compounds in the blood were negative.

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<sup>1</sup> Stokes, J. H., Beerman, H., and Ingraham, N. R. Photodynamic Effects in Dermatology, *Am J M Sc* 204: 601 (Oct) 1942.

On January 29 the patient received a total of 50,000 units of penicillin in divided doses of 10,000 units every three hours. On January 30 he took a sun bath in the afternoon. At night an erythema was noticed on the areas previously exposed to the sun. This persisted in a rather severe form until February 2. On February 3 the diffuse erythema had subsided considerably, but a morbilliform eruption was noted on the back, chest and face and on the extensor aspect of the extremities. These areas were more severely affected by the sunburn than the rest of the body surfaces. The lesions were macules and varied in size from that of a match head to that of a lentil. They had a tendency to become confluent. The mucous membranes were not involved. There was no generalized or localized adenopathy. The temperature was normal. A hemogram on February 3 was normal. On February 4 the eruption had become more profuse. On February 5 it showed definite signs of improvement. It was still localized to the areas previously exposed to sunlight. The area not exposed to actinic rays was entirely free of lesions. On February 6 the patient was discharged, as the eruption had faded considerably and his urethral discharge had disappeared.

## COMMENT

It is possible that the photosensitivity in this case was produced by the sulfonamide compounds previously administered, but this is unlikely, as fifteen days had elapsed since the administration of the drug and tests of the blood showed no residual sulfadiazine prior to the administration of penicillin. Besides, the patient stated that he had had at least three sun baths since the use of sulfadiazine was discontinued, without any abnormal reaction. The appearance of a morbilliform eruption in the same areas previously affected by a sunburn four days after treatment with penicillin strongly suggests the possibility that this drug had acted as a photosensitizing agent.

# MYCOSIS FUNGOIDES IN THE NEGRO

HARRY SIGEL, M.D.

CINCINNATI

Mycosis fungoides is uncommon in the Negro. There are only a few scattered case reports in the literature, and discussions at various dermatologic societies indicate that the disease is rarely seen in members of that race.

In August 1943 reports of 2 such cases were published in the Transactions of the Chicago Dermatological Society, one by Ebert and Otsuko<sup>1</sup> and the other by Mitchell and Scull.<sup>2</sup> In discussing these cases, Stillians<sup>3</sup> remarked that he had observed only 1 other case. Oliver,<sup>4</sup> on the other hand, noted that up to a few years previously the disease was rather uncommon in the Negro but that in the last few years he had seen a number of them with the disease. Ebert<sup>1</sup> stated that the patient whom he presented was the second Negro with mycosis fungoides that he had ever seen. Mitchell<sup>2</sup> also stated that the disease was thought to be rare in that race. In September 1943 Mitchell and Scull<sup>2</sup> presented another Negro with probable mycosis fungoides. Wile,<sup>5</sup> in discussing this case stated that he did not recall having seen mycosis fungoides in a Negro. Nicholas<sup>6</sup> also presented a possible case of mycosis fungoides in a Negro.

An average of 359 patients are admitted yearly to the dermatologic service of the Cincinnati General Hospital, 48 per cent of whom are Negroes. Although 3 Negroes with mycosis fungoides have been observed in this service in the past twelve years, the records for only 2 of them are complete, they are presented in

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1 Ebert, M. H., and Otsuko, M. Mycosis Fungoides in the Tumor Stage, Arch. Dermat. & Syph. 48: 214 (Aug.) 1943.

2 Mitchell, J. H., and Scull, R. H. A Case for Diagnosis (Mycosis Fungoides), Arch. Dermat. & Syph. 48: 213 (Aug.) 1943.

3 In discussion on papers of Ebert and Otsuko, Mitchell and Scull and Oliver and Bluefarb, Arch. Dermat. & Syph. 48: 215 (Aug.) 1943.

4 Mitchell, J. H., and Scull, R. H. Mycosis Fungoides, Arch. Dermat. & Syph. 48: 353 (Sept.) 1943.

5 Wile, U. J., in discussion on Mitchell and Scull.<sup>4</sup> p. 354.

6 Nicholas, L. Mycosis Fungoides, Arch. Dermat. & Syph. 49: 291 (April) 1944.

this paper. During the same period 4 white patients with mycosis fungoides were admitted.

CASE 1—M. S., a 29 year old Negro woman, was admitted to the dermatologic service of the Cincinnati General Hospital on Sept. 12, 1931, complaining of a persistent generalized eruption of one year's duration. She had been treated locally with ointments, without relief, and had received seventy treatments with high voltage roentgen rays, with some temporary relief. The lesions, however, frequently recurred in the scalp after the roentgen ray therapy.

*Past History*—In early infancy she had an eruption on her hands which her parents called "eczema" and which cleared up with local treatment. At the age of 9 she had "ringworm" of her face and was benefited by tincture of iodine. Shortly afterward lesions appeared on her buttocks and spread over her back. These lesions persisted, and from time to time in the years following there were sporadic outbreaks on the extremities.

There was no known personal or family history of syphilis, but there had been a spontaneous abortion a few years previously. The patient had had pneumonia the previous year but no signs or symptoms of tuberculosis. There was no personal or family history of any type of allergy.

*Physical Examination*—The patient was an obese young Negro woman, appearing neither acutely nor chronically ill. There was no cyanosis, dyspnea, icterus, pallor or edema of the extremities, there were no petechiae.

Examination of the skin revealed an extensive eruption from head to toes. It was of an essentially chronic nature and included many types of lesions. The early lesions were observed on the forearms in extensive groups of small maculopapular and small pustular lesions. On the scalp there were a few circular crusted areas. The skin of the face was thickened and scarred about the nose and mouth, giving the face a suggestive leonine appearance. Some scarring and desquamation were present about the ears. On the trunk and extremities were numerous raised circular lesions, these either were scarred entirely or were partially scarred, the remainder of the surface being covered with thick whitish crusts. Areas of lichenification were present in the flexural surfaces. On the dorsal areas were lesions of varying sizes and shapes covered with thick whitish scales, some of them "psoriasis-like." There were flat superficial areas of desquamation on the palms and over the feet. Over the trunk and extremities there were scattered numerous deeply pigmented smooth areas. The labia were thickened and whitish. There were no lesions in the vagina, mouth or pharynx.

The rest of the physical examination revealed essentially normal conditions, save for a basal systolic murmur on auscultation of the heart.

*Laboratory Data*—The red blood cell count varied between 4,300,000 and 3,400,000 with 60 to 70 per cent hemoglobin (Tallqvist). The leukocyte and differential counts were normal, and no eosinophils or pathologic blood cells were found. Results of urinalysis were normal. Scrapings of the lesions failed to grow fungi. Serologic tests of the blood elicited negative reactions. A series of roentgenograms of the gastrointestinal tract were reported as showing essentially normal conditions.

Biopsy of skin taken from one of the lesions was reported by the pathologists as indicating mycosis fungoides. The section showed parakeratotic crusting and occasional areas of follicular plugging. There was acanthosis almost palisade in type, with deep rete plugs and intercellular bridges. There was spotty pigmentation of the basal layer, with numerous areas of vacuolation and degeneration, and an extensive cellular infiltrate extended over the pars papillaris deep down to the pars reticularis. This infiltrate was made up of dense or close-packed cells, consisting of lymphocytes, plasma cells, eosinophils and large multinucleated giant cells with deeply staining nuclei. Scattered through

and ileum, slight diffuse fibrosis of the adrenal glands and early generalized arteriosclerosis.

CASE 2—M. D., a 56 year old Negro woman, was first seen in the dermatologic clinic at the Cincinnati General Hospital on Sept 14, 1943. She complained of a generalized pruritus of about one year's duration. Itching started on the hands and subsequently spread to the arms, legs and body. The patient excoriated her skin, and these areas became irritated, bled and crusted and finally became thickened and lichenified.

There was a past history of hypertension, cholecystectomy about seven years previously and a rectal fissure twenty years previously.

Physical examination of the skin revealed thickened, raised, deeply pigmented plaques covered with fine scales of various sizes and of round or oval shape (the figure). The thicker plaques, with elevated well defined borders, were found on the mesial surfaces of the thighs and on the under side of the upper arms. There were smaller lesions on the hands. On the face the lesions were smaller and flatter and with less



Early tumor phase of mycosis fungoides (case 2)

the cellular infiltrate were numerous chromatophores. The collagen fibers showed fragmentation and separation. Glands and blood vessels showed no changes.

A diagnosis of the tumor phase of mycosis fungoides was made.

The patient's course was downhill while she was in the hospital. She received numerous roentgen ray treatments, with only temporary relief. She gradually began to depend more and more on morphine and scopolamine for relief of pain. Her condition slowly became worse, with severe weakness and cachexia. She died on March 29, 1932 and a postmortem examination was made.

At necropsy the conditions observed were mycosis fungoides changes of the lymph nodes and skin, pulmonary congestion and edema, with areas of lobar pneumonia and infarction, congestion of the spleen, with moderate proliferation of the reticuloendothelial system, toxic nephrosis, chronic passive congestion of the liver, with moderate atrophy of the hepatic cords, toxic hepatitis, with pronounced fatty infiltration, thrombosis of the veins of the bladder, toxic myocarditis, decided postmortem changes of the pancreas

definite margins. There were few lesions on the back, and these were flat, pigmented and slightly scaly.

There was some scaling in the interdigital spaces of the feet.

The rest of the examination revealed normal conditions with the exception of the cardiovascular system. The patient had hypertension (blood pressure of 160 systolic and 70 diastolic), and a precordial systolic murmur was heard more over the base of the heart, loudest in the second right interspace.

*Laboratory Data*—The red and white blood cell counts and the differential count were always within normal limits. The report of hematologic consultation, for the study of blood smears stated that the findings were not diagnostic of any particular syndrome and were consistent with any subacute disease.

Results of examinations of the urine were consistently normal.

Scrapings of scales from the lesions showed no growth on Sabouraud's medium. A trichophytin test elicited a negative reaction. A roentgenogram of the chest showed no infiltration and no enlargement of hilar nodes. Biopsy of the skin from one of the



involved areas showed spongiosis, parakeratosis and intraepidermal vesicles. There was edema of the dermis, with scattered perivascular infiltrate of plasma cells and eosinophils. An eczematoid reaction was suspected from the biopsy.

The patient had an uneventful course in the hospital except for an unexplained fever which lasted about ten days. The lesions improved with local medication and low voltage roentgen ray therapy. She was discharged in October 1943 with no definite diagnosis, although the premycotic stage of mycosis fungoides as well as an allergic eczematoid dermatitis was suspected.

The patient returned to the clinic two months later with a pronounced exacerbation of her lesions and was readmitted to the ward. There were many crusted oozing lesions scattered on all parts of the body and ranging from the size of a dime to that of a silver dollar. Some of the areas were confluent and formed even larger lesions.

A biopsy of the skin from an involved area was made. The section showed extensive acanthosis with numerous long rete plugs with some intercellular bridging. The basal cell layer showed some vacuolation and considerable loss of basal cell pigment. There were occasional areas of chromatophore pigment. Dense cellular infiltrate was present, extending in large sheetlike masses throughout the entire dermis. This infiltrate was composed of densely packed lymphocytes, polymorphonuclear cells, eosinophils and multinucleated

large cells. Large cells with pale bluish nuclei were also observed. Blood vessels showed no remarkable changes.

A diagnosis of the tumor phase of mycosis fungoides was made.

The patient was then given many roentgen ray treatments, which gradually improved her enough to enable her to go home.

CASE 3—No detailed records are available on this third case save a brief report of the patient's presentation before the Cincinnati Society of Dermatology and Syphilology. She was admitted in the tumor phase of mycosis fungoides, with typical biopsy findings, and died while in the hospital. The diagnosis of mycosis fungoides for this Negro woman was accepted by the society.

The clinical features in these cases were in no ways different from the picture in cases of mycosis fungoides in white patients.

#### CONCLUSIONS

In a study of 3 cases of mycosis fungoides in Negro patients, no special clinical or histological differences between mycosis fungoides in white and in Negro patients could be made out.

# DERMATOLOGIC PRACTICE IN A STATION HOSPITAL IN SOUTHERN CALIFORNIA

A COMPARISON WITH PRIVATE PRACTICE

CAPTAIN ERVIN EPSTEIN

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It should be obvious that practice of medicine in the Army differs from that in civilian life. The reasons for this are multiple. Even if the factors of trauma and tropical dermatoses are eliminated, the cutaneous diseases studied in an Army hospital are not identical with those seen in peacetime. The type of patient observed determines the cutaneous changes encountered. In the Service, one is dealing with healthy young men. Therefore, one should expect an increase in the diseases commonest in this group, with an absolute or relative absence of dermatoses peculiar to children, women and persons of advanced age. The relatively crowded living facilities would be expected to encourage the spread of contagious diseases. The dermatologist would be called on to treat certain dermatoses seldom seen in his civilian practice, including, as an example, sunburn. This is due to the fact that persons with sunburn are seldom referred by the general practitioner to the specialist in diseases of the skin.

To confirm or disprove this conception, 1,280 patients seen in a station hospital in Southern California were compared with the last 1,280 patients treated in civilian life. In the former group, a total of 1,519 diagnoses were made while in the latter series, 1,607 diseases were encountered. Among the civilian patients, only 283 per cent were eligible for military service by virtue of their age and sex. Although some of the older officers and families of the officers or enlisted men were included in the Army group, over 95 per cent of the patients were men ranging in age from 18 to 38 years.

## RELATIVE FREQUENCY OF DERMATOSES

Table 1 shows the 20 most common cutaneous diseases encountered in the Army series. The incidence in the civilian group is included to provide a ready basis for comparison. Table 2 demonstrates the 20 commonest dermatoses seen in private practice as compared with the inci-

dence of the given diseases in the Army group. A study of these tables offers certain interesting facts.

TABLE 1—Incidence of Most Common Dermatoses in Service Series Compared with Incidence in Civilian Group

| No | Dermatoses               | Army     |          | Num<br>ber | Civilians |          |
|----|--------------------------|----------|----------|------------|-----------|----------|
|    |                          | Patients | Per Cent |            | Patients  | Per Cent |
| 1  | Dermatophytosis          | 239      | 16.8     | 5          | 96        | 7.5      |
| 2  | Eczema                   | 204      | 15.9     | 4          | 99        | 7.7      |
| 3  | Dermatitis venenata      | 145      | 11.3     | 1          | 278       | 21.6     |
| 4  | Verrucae                 | 115      | 9.0      | 6          | 76        | 5.9      |
| 5  | Scabies                  | 93       | 7.2      | 11         | 39        | 3.0      |
| 6  | Aene vulgaris            | 70       | 5.5      | 3          | 100       | 7.7      |
| 7  | Dermatitis actinica      | 56       | 4.7      |            | 1         | 0.08     |
| 8  | Seborrheic dermatitis    | 47       | 3.7      | 2          | 136       | 10.6     |
| 9  | Impetigo contagiosa      | 47       | 3.7      | 8          | 47        | 3.7      |
| 10 | Psoriasis                | 38       | 2.9      | 12         | 35        | 2.7      |
| 11 | "Bites"                  | 29       | 2.3      | 16         | 22        | 1.7      |
| 12 | Nevi                     | 27       | 2.1      | 13         | 33        | 2.6      |
| 13 | Tinea versicolor         | 25       | 1.9      |            | 6         | 0.5      |
| 14 | Urticaria                | 23       | 1.8      | 18         | 20        | 1.6      |
| 15 | Pityriasis rosea         | 23       | 1.8      | 10         | 41        | 3.2      |
| 16 | Diseases of sweat glands | 23       | 1.8      |            | 4         | 0.3      |
| 17 | Pyoderma                 | 16       | 1.2      |            | 9         | 0.7      |
| 18 | Syphilis (primary)       | 15       | 1.2      |            | 1         | 0.08     |
| 19 | Furunculosis             | 14       | 1.1      | 16         | 23        | 1.8      |
| 20 | Herpes simplex           | 14       | 1.1      |            | 16        | 1.2      |

The heading "Number" refers to position in civilian list, as dermatophytosis is no. 1 in Army list but fifth among civilians.

TABLE 2—Incidence of Most Common Dermatoses in Civilian Group Compared with Incidence in Service Series

| No | Dermatoses                | Civilians |          | Num<br>ber | Army     |          |
|----|---------------------------|-----------|----------|------------|----------|----------|
|    |                           | Patients  | Per Cent |            | Patients | Per Cent |
| 1  | Dermatitis venenata       | 278       | 21.6     | 3          | 145      | 11.3     |
| 2  | Seborrheic dermatitis     | 136       | 10.6     | 8          | 47       | 3.7      |
| 3  | Aene vulgaris             | 100       | 7.7      | 6          | 70       | 5.5      |
| 4  | Eczema                    | 99        | 7.7      | 2          | 204      | 15.9     |
| 5  | Dermatophytosis           | 96        | 7.5      | 1          | 239      | 16.8     |
| 6  | Verrucae                  | 76        | 5.9      | 4          | 115      | 9.0      |
| 7  | Keratosis                 | 52        | 4.1      |            | 10       | 0.8      |
| 8  | Impetigo contagiosa       | 47        | 3.7      | 9          | 47       | 3.7      |
| 9  | Epitheliomas              | 41        | 3.2      |            | 7        | 0.5      |
| 10 | Pityriasis rosea          | 41        | 3.2      | 15         | 23       | 1.8      |
| 11 | Scabies                   | 39        | 3.0      | 5          | 93       | 7.2      |
| 12 | Psoriasis                 | 35        | 2.7      | 10         | 38       | 2.9      |
| 13 | Nevi                      | 33        | 2.6      | 12         | 27       | 2.1      |
| 14 | Furunculosis              | 23        | 1.8      | 19         | 14       | 1.1      |
| 15 | Angiomas                  | 22        | 1.7      |            | 2        | 0.16     |
| 16 | "Bites"                   | 22        | 1.7      | 11         | 29       | 2.3      |
| 17 | Dermat medicamentosa      | 21        | 1.6      |            | 8        | 0.6      |
| 18 | Urticaria                 | 20        | 1.6      | 14         | 23       | 1.8      |
| 19 | Sycosis vulgaris          | 18        | 1.4      |            | 12       | 0.9      |
| 20 | Pruritus ani et/or vulvae | 17        | 1.3      |            | 7        | 0.56     |

The tables indicate that certain diseases are more common in the Army, including superficial mycoses, eczema, verrucae, scabies, dermatitis

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actinica and diseases of the sweat glands. On the other hand, many were seen more frequently among civilians, including contact dermatitis, seborrheic dermatitis, epitheliomas and keratoses. Rosacea was fourteen times as common in the civilian group. In a few, there was little or no difference, as exemplified by impetigo contagiosa, psoriasis, urticaria, herpes simplex and zoster. The reasons for the discrepancies between the two series will be discussed later.

Although 94 different diagnoses were made in the Army group and 137 in the civilian group, a study of the tables indicates that more than three fourths of the cases fell within the 20 most common conditions in each series. Among the Army patients, 63.5 per cent were accounted for by the first 10 diagnoses and an additional 13.2 per cent by the next 10, a total of 76.7 per cent. Among the civilians, the 10 most frequent diagnoses included 60.3 per cent and the subsequent 10, 15.5 per cent for a total of 75.8 per cent of the patients. This reiterates the importance of a thorough knowledge of the everyday conditions in the successful practice of dermatology.

A consideration of the rare lesions show a greater frequency among the civilians (35 to 11). This is to be expected because of the more varied material. Civilians included patients with idiopathic calcinosis cutis, eczema vaccinatum, multiple benign cystic epithelioma, erythema diutinum, erythroplasia of Queyrat, exfoliative erythroderma, folliculitis decalvans, glomus tumor, glossitis rhomboidea mediana, lichen sclerosus et atrophicus, lupus vulgaris, lymphatic leukemia cutis, necrobiosis lipoidica diabetorum, pemphigus, pigmented stripe of the nail, pseudo atrophoderma colli, pseudopelade, pseudo xanthoma elasticum, purpura annularis telangiectodes, giant cell sarcoma, fibroblastic sarcoma, idiopathic hemorrhagic sarcoma of Kaposi, sarcomoid, other tuberculids, dermatitis herpetiformis and parapsoriasis. In the Army, only dermatitis herpetiformis, keratosis follicularis, parapsoriasis, ectodermosis erosiva pluriorificialis, xeroderma pigmentosum, angioma serpiginosum and leprosy were observed. As I have stated the common dermatoses are the most important but familiarity with the unusual conditions is essential for the proper development of a dermatologist.

The opportunities for surgical experience must also be considered. The dermatologist in the Army has an opportunity to improve his technic by working with competent surgeons. However, he lacks patients with the wide variety of diseases that can be treated by surgical means.

Table 3 shows the dermatoses treated by surgical approaches in Army personnel and in civilians. The most important lack in the Army is the opportunity to treat the important malignant and premalignant diseases. This is explained by the ages of the men under consideration. Of the diseases presented by the soldiers 11.2 per cent were treated by surgical or electro-surgical means as compared with 19.8 per cent in the civilians. An equal number of warts was removed in each group, but due to the fact that nearly twice as many operations were performed on the civilians, the percentage of total operations for removal of verrucae was twice as great.

TABLE 3—*Dermatoses Treated Surgically in Service Series Compared with Those in Civilian Group*

| No | Condition Treated                              | Army  |          | Civilians |          |
|----|--|-------|----------|-----------|----------|
|    |  | Cases | Per Cent | Cases     | Per Cent |
| 1  | Verrucae                                       | 68    | 47.5     | 62        | 24.4     |
| 2  | Nevi   | 18    | 12.6     | 31        | 12.2     |
| 3  | Sebaceous cysts                                | 13    | 9.1      | 7         | 2.8      |
| 4  | Abscess (incision)                             | 11    | 7.7      | 4         | 1.6      |
| 5  | Biopsy   | 9     | 6.3      | 7         | 2.8      |
| 6  | Keratoses                                      | 6     | 4.2      | 52        | 20.2     |
| 7  | Acne (desiccation)                             | 6     | 4.2      | 0         |          |
| 8  | Onychectomy                                    | 5     | 3.5      | 5         | 1.2      |
| 9  | Foreign body granuloma                         | 4     | 2.8      | 0         |          |
| 10 | Epitheliomas                                   | 3     | 2.1      | 40        | 15.7     |
| 11 | Granuloma pyogenicum                           | 5     | 2.1      | 4         | 1.6      |
| 12 | Angiomas                                       | 2     | 1.4      | 8         | 3.1      |
| 13 | Fibroma  | 1     | 0.7      | 7         | 2.8      |
| 14 | Lipoma   | 1     | 0.7      | 1         | 0.4      |
| 15 | Folliculitis keloidalis                        | 1     | 0.7      | 2         | 0.8      |
| 16 | Lymph node incision                            | 1     | 0.7      | 0         |          |
| 17 | Cutaneous horn                                 | 1     | 0.7      | 8         | 3.1      |
| 18 | Epithelial cyst                                | 1     | 0.7      | 1         | 0.4      |
| 19 | Melanoma                                       | 1     | 0.7      | 1         | 0.4      |
| 20 | Neurofibroma                                   | 1     | 0.7      | 0         |          |
|    | Leukoplakia                                    | 0     |          | 6         | 2.4      |
|    | Sarcoma  | 0     |          | 5         | 1.2      |
|    | Molluscum contagiosum                          | 0     |          | 2         | 0.8      |
|    | Chondrodermatitis nodularis chronica helioides | 0     |          | 1         | 0.4      |
|    | Multiple benign cystic epithelioma             | 0     |          | 1         | 0.4      |
|    | Glomus tumor                                   | 0     |          | 1         | 0.4      |
|    | Lupus vulgaris                                 | 0     |          | 1         | 0.4      |

in the Service. Twice as many moles were removed from civilians. Nevi are mainly a cosmetic problem and therefore one that women would give more attention to than do fighting men. The increase in sebaceous cysts in the Service is more apparent than real. Surgeons, general practitioners and others in civilian life remove many of these lesions without referring them to a dermatologist. The removal of degenerative and malignant lesions is more common in civilians for often repeated reasons. Included in this group are keratoses, cutaneous horns, leukoplakia, epitheliomas and sarcomas. Angiomas are usually seen in infants or persons of advanced age, hence the comparative absence in the Service series of cases.

## SPECIAL PROBLEMS IN THE ARMY

In the ultraspecialization of an Army hospital, the dermatologist is confronted by certain problems of organization and supply that do not exist in his own office. For instance, all ultraviolet radiation therapy is administered by the physical therapy department. While it is prescribed by the dermatologist, it is not administered by him, which leads to certain complications. In some hospitals, dermatologic surgical procedures are performed by general surgeons. Roentgen ray therapy is not available in station hospitals and is controlled by the radiologist in general hospitals. Furthermore, the radiologic diagnostic case load is so great as to preclude radiotherapy for comparatively innocuous dermatoses.

It is necessary for the dermatologist to engage in certain activities foreign to his usual routine. This includes military duties, administrative details, preparation of forms, maintenance of discipline and a certain amount of general practice in assuring each patient in the hospital of a

TABLE 4—*Superficial Mycoses Seen in Service Series*

| No | Type                     | Cases | Per Cent |
|----|--------------------------|-------|----------|
| 1  | Dermatophytosis          | 151   | 63.2     |
| 2  | Tinea cruris             | 71    | 29.7     |
| 3  | Tinea versicolor         | 25    | 10.4     |
| 4  | Involvement of hands     | 13    | 5.4      |
| 5  | Onychomycosis            | 11    | 4.6      |
| 6  | Tinea corporis           | 8     | 3.3      |
| 7  | Natal cleft and buttocks | 6     | 2.5      |
| 8  | Tinea barbae             | 4     | 1.7      |
| 9  | Tinea capitis            | 2     | 0.8      |
| 10 | Involvement of axillae   | 1     | 0.3      |
| 11 | Erythrasma               | 1     | 0.3      |
| 12 | Majocchi's granuloma     | 1     | 0.3      |

complete medical examination. Special duties as officer of the day, physical inspection for contagious diseases, medical officer on troop maneuvers, etc., further diversify his activities.

Life in the service modifies the type of diseases treated, and some of the more common ones will be considered at this time.

**Dermatophytosis** The commonest dermatoses seen in the Army are those due to superficial mycotic infections. Such diseases are more than twice as common as in private practice. Table 4 gives the incidence of the various types encountered in the service.

As expected, "athlete's foot" is the most common manifestation. However, the incidence of tinea cruris, which comprises nearly 30 per cent of the dermatomycoses, is surprising. The sex and age of the patients involved are probably potent factors in explaining this. An incidence of tinea versicolor of 10 per cent in this group also seems excessive. It cannot be explained by conditions in the Army, because the eruption antedated induction into the Service in all cases.

Involvement of the hands by a true local mycotic infection occurred in 5.4 per cent of the cases. This roughly confirms the findings presented in a previous paper,<sup>1</sup> although the basis for determining the incidence varied. The fact that not one case of primary vesicular dermatophytosis of the hands was encountered is of importance. It was demonstrated in the previous study that this form occurs only in women. All of the cases in the Army were of the desquamative or hyperkeratotic type.

Onychomycosis was common. In 1 patient, 15 nails were involved. In another, seen at a different station hospital and not included in this compilation, all 20 nails were involved and were avulsed under general anesthesia. Onychomycotic involvement of the hands was often accompanied by a hyperkeratotic trichophytosis of the hands. *Trichophyton purpureum* was a frequent offender in this respect.

Despite the age of the patients, tinea corporis and tinea capitis were occasionally seen. The 4 cases of tinea barbae were a surprise, as this disease is encountered rarely on the Pacific coast. All of these patients were from the Middle West. It might also be mentioned that involvement of the natal cleft and buttocks was not infrequent, especially in association with tinea cruris.

**Eczema** Atopic eczema was the second most common dermatosis. Most of the patients recounted a long history of repeated relapses with induction into the Army while the disease was in a quiescent state. Many received medical discharges because of recurrences after short periods of service. One often hears the statement that such patients do well with a change of environment. The desert is recommended particularly. This series disputes the value of such advice. Most of the patients came from the Middle West, and the change to the Pacific coast was usually of no benefit. Furthermore, the majority became worse on the deserts of Southern California.

**Dermatitis Venenata**—Most of these eruptions were due to leather, wool, soap, metals, grease and oil. Of course, nail polish dermatitis was not seen. Since most patients received prompt, adequate treatment, there was a dearth of dermatoses due to self medication. This was a welcome change from the overtreated civilian. Many examples of leather and wool dermatitis were seen. In the former group, perspiration seemed to precipitate the eruption. Trichophytosis also acted as a contributory factor when

1 Epstein, E. Dermatophytosis of the Hands. Diagnosis and Prognosis, Arch Dermat & Syph 15: 1113 (June) 1942.

the feet were involved. Wool dermatitis often followed scabies and sulfur dermatitis. In both leather and wool allergies, the eruption and sensitivity tended to be comparatively persistent. Eruptions due to metal were usually caused by identification tags worn on the chest. Some of the men employed plastic strings to suspend the tags around the neck. These plastics proved to be allergenic in some instances.

*Verrucae*—In about 20 per cent of the patients treated by local applications, such as tincture of iodine, the lesions cleared without surgical intervention. However, curettage followed by chemical cauterization was the most efficacious method employed.

*Scabies*—The incidence of scabies is probably no greater than that encountered in a clinic practice. In most cases in civilian life this disease is diagnosed and treated by the general practitioner. Hence, the percentage seen by the dermatologist is greater among soldiers.

*Acne Vulgaris*—The greater incidence of acne vulgaris in civilian practice is due to the inclusion of females in that group. Adolescent girls are more concerned with cosmetic problems than are boys. Therefore, they are more apt to seek medical care than the man with the same disfiguring complaint. Roentgen ray therapy was not available, but therapeutic results following use of a simple face lotion were comparatively good. This is assumed to be due to the active outdoor life led by the soldiers in a training camp.

*Dermatitis Actinica*—Eruptions due to exposure to the sun were common. The camp is located on the seashore. No such eruptions were encountered in a similar hospital in the desert. During the summer months, the men would lie on the beach for from one to four hours on Sunday. This resulted in many severe burns, 52 of the 56 listed requiring hospitalization. Constitutional symptoms included fever, malaise, nausea, vomiting and, in 1 case, anuria. In some patients, large bullae extending deep into the dermis were found to be filled with coagulated serum. In addition to the cases of sunburn, there were 6 patients with eruptions considered to be due to solar sensitivity. In 4 the eruption was of the eczematoid type and in 1, urticarial. The sixth patient presented sarcoid-like nodules that cleared on hospitalization and recurred promptly on exposure to sunlight. There were also 11 patients with severe inflammation of the lower lip. In 3, the lower lip was replaced by exuberant granulation tissue. Therapy consisted of hospitalization and repeated cauterization with fused silver nitrate. Protective oint-

ments containing tannic acid and phenyl salicylate were ineffective in preventing recurrences in patients with photosensitivity and/or cheilitis. It was interesting that the cheilitis did not in any instance coexist with a severe sunburn.

*Psoriasis*—While the incidence of this disease was practically identical in the two groups, other factors make it noteworthy. Every case of psoriasis, except 1, became accentuated or precipitated in the Army. Of course, Army life is filled with psychic conflicts and annoyances to the individual. It is believed that these factors aggravated the disease. It was also found that this dermatosis responded well if treated with ultraviolet radiation plus the internal use of sulfanilamide and/or a crude coal tar paint applied locally.

*Hyperhidrosis, Dysidrosis and Bromhidrosis*—Manifestations of increased or altered activity of the sweat glands were more common in the Army, because the soldiers lead a more strenuous life than the average civilian. Involvement of the palms and soles was frequently encountered. All of these disturbances were particularly common in troops in the desert in summertime.

*Keratosis and Epitheliomas*—The oft-accentuated age factor prevented more cases of these diseases from appearing in the Army. However, several cases of malignant disease are worthy of mention. In a 23 year old woman, wife of an enlisted man, a basal cell epithelioma developed on the root of her nose in a patch of lupus erythematosus. The preceding eruption was of two years' duration. A 60 year old woman, wife of an officer, had her left breast removed because of cancer five years before examination. She presented five superficial basal cell epitheliomas on her right breast. A 32 year old enlisted man presented a basal cell epithelioma of the left lower eyelid of five years' duration. No sarcomas were encountered. It is believed that the 3 sarcomas seen among the private patients represent an abnormally high incidence. In addition there were 2 instances of idiopathic hemorrhagic sarcoma of Kaposi in the group from private practice.

*Rosacea*—Only 1 case of rosacea was seen in the Army. The patient presented a severe eruption of the pustular type. In comparison, there were 14 civilians with this disease. This is not surprising when one considers that rosacea is predominantly a disease of middle-aged women.

*Seborrheic Dermatitis*—The only explanation that I can offer for the increased incidence among civilians is that "dandruff" is a minor ailment

which seldom worries the healthy young man. On the other hand, women are distressed by flakes of "dandruff" on their shoulders. There were no cases of seborrhea nochum among the soldiers, further increasing the difference.

*Pyodermas* The incidence of infections of the skin due to streptococcus and/or staphylococcus was not excessive. The combined incidence of impetigo contagiosa, ecthyma, furunculosis, folliculitis, cellulitis, sycosis vulgaris and paronychia was only 7.6 per cent. In private practice, these diagnoses were made for 11.8 per cent of the patients. The comparatively low incidence could be explained by the cleanliness that the Army insists on.

*Venereal Diseases*—The incidence of active venereal diseases included 15 cases of primary syphilis, 10 of secondary syphilis and 4 of lymphogranuloma venereum (a total of 29 cases). This far exceeds the 1 patient with a chancre, 3 with secondary infections and none with lymphogranuloma in the civilian group. However, the increased incidence among the soldiers is also more apparent than real. The frequent inspections and regulations concerning

such matters force the man in the Service to report for early diagnosis and treatment. Therefore, fewer cases reach latency. Furthermore, all of the cases of syphilis are concentrated in one department rather than being diffused through every office in a given community.

*Self-Induced Dermatoses* It is worthy of mention that but 2 instances of neurotic excoriations, both in morons, were seen in the Army. In addition, 1 patient who resented being in the Army had a self-inflicted dermatitis. This is an extremely low incidence indeed.

#### SUMMARY

1 The incidence of cutaneous disease in 1,280 soldiers as compared with the incidence of such diseases in 1,280 patients seen in private practice showed that fungous infections, eczema, verrucae, scabies and dermatitis actinica are encountered more frequently in soldiers than in civilians. On the other hand, keratoses, epitheliomas, rosacea, seborrheic dermatitis and dermatitis venenata are seen less often in this group.

2 Sex, age and environment have an influence on this difference in occurrence.

# CUTANEOUS LEISHMANIASIS (ORIENTAL SORE)

## VI TREATMENT WITH QUINACRINE HYDROCHLORIDE

D A BERBERIAN, MD

BEIRUT, LEBANON

Flarer<sup>1</sup> (1938) stated that solution of quinacrine hydrochloride injected into the skin around oriental sore rapidly destroyed the parasites and cured the disease. He recommended one to four injections of 0.05 to 0.1 Gm of quinacrine hydrochloride dissolved in 1 or 2 cc of distilled water to be given at the first treatment and the quantity to be increased at subsequent treatments to 0.3 Gm. He also stated that with this treatment in some cases a single injection was sufficient to bring about a cure. He reported on the use of the treatment in 14 cases. The same method of treatment was used in a few cases by Cupi and Cattapan<sup>2</sup> (1942) in Eritrea, with satisfactory results. Dobrotvorskaya<sup>3</sup> (1941) elaborated the treatment originally introduced by Flarer and varied it according to the type and age of lesions. He claimed that the early dry type of papules could be destroyed with a 5 per cent solution of quinacrine hydrochloride if it was injected at several points around the papule. He treated the ulcerated sores by infiltration with 5 to 10 cc of a 3 per cent solution and applied locally an ointment of 10 per cent quinacrine hydrochloride as well as an ointment of 2-ethoxy-6,9-diaminoacridine lactate (rivanol) and another of strong protein silver (protargol). He admitted that none of the modifications that he introduced produced complete cures though in all cases he observed considerable improvement. Mazza and Cornejo<sup>4</sup> (1940) used Flarer's

method in the treatment of American leishmaniasis. They infiltrated the sore with 5 cc of a 10 per cent solution of quinacrine hydrochloride and at the same time gave 3 tablets of 0.1 Gm each daily for seven days. They obtained good results with unbroken cutaneous lesions but mucosal lesions failed to respond to this treatment. For the latter, they recommended combined stibophen and chiniofon medication. Marchionni<sup>5</sup> (1941) reported on the treatment in 300 cases, in which he used 1 to 2 cc of a 10 to 20 per cent solution of quinacrine hydrochloride. Local injections were repeated 2 or 3 times at eight to ten day intervals. He used intravenous and intramuscular injections of 0.1 to 0.3 Gm for multiple sores. He obtained good results in early stages but failed to effect a cure in many cases of atypical and chronic leishmaniasis, especially in the stage when leishmanias could not be found in the lesions.

I attempted to try out the effectiveness of Flarer's method of treatment on the artificial sores that were produced on volunteers. These sores were produced on the anterior aspects of the thighs about 15 cm above the knee cap, by the intracutaneous injection of 0.2 cc of a suspension of *Leishmania tropica* containing approximately 200,000 leishmanias. The following results were obtained.

### EXPERIMENTAL STUDIES

EXPERIMENT V-64—A one hundred and seventy-two day old artificially induced sore, nonulcerated and about 12 mm in diameter, was treated with 1, 2 and 3 cc doses of a 10 per cent solution of quinacrine hydrochloride given at weekly intervals. The first two injections were well tolerated, but the third injection gave a well defined local inflammatory reaction, about 15 cm in diameter, associated with some fever (temperature 101.3 F [38.4 C]) and malaise. The lesion swelled and began to ulcerate. The inflammation gradually subsided, leaving a large ulcer which healed slowly by granulation and left a scar 4 cm in diameter.

Local infiltration with a 10 per cent solution of the drug did not favorably alter the course of the sore but precipitated early ulceration and enlarged the sore, which on healing left a scar 25 by 30 mm in diameter.

5 Marchionni, A. Die Behandlung der Orientbeule, Schweiz med Wchnschr 71 1220-1223, 1941

From the Department of Parasitology, the American University of Beirut

1 Flarer F. Nuovo methodo di cura per la leishmaniosi cutanea (bottomi d'oriente), Boll d Ist sieroterap milanese 18 469-473, 1938

2 Cupi, N., and Cattapan, A. Contributo allo studio del bottone d'oriente nel governo dell'amara, Boll Soc ital di med e ig trop 1 19-24, 1942 abstracted Trop Dis Bull 40 124, 1943

3 Dobrotvorskaya, N V. Treatment of Cutaneous Leishmaniasis, in Problems of Cutaneous Leishmaniasis, Ashkabad, pp 207-226 (in Russian, with French summary, p 301) Hoare C A. Cutaneous Leishmaniasis (Critical Review of Recent Russian Work), Trop Dis Bull 41 331-345, 1944.

4 Mazza, S., and Cornejo, A. Ensayos de atebina en leishmaniosis tegumentaria americana. Prensa med argent 27 1734-1736, 1940

EXPERIMENT V-75—A one hundred and fifty-seven day old artificially produced oriental sore 12 mm in diameter and nonulcerated was treated with a 10 per cent solution of quinacrine hydrochloride. Two doses (1 and 2 cc) were given one week apart. The second injection was followed within a few hours by an intense local reaction, without fever. Because of the local reaction, injections were discontinued. The lesion took its regular course and was not affected by the injections of quinacrine.

EXPERIMENT V-77—A one hundred and fifty-seven day old artificially produced nonulcerated oriental sore about 12 mm in diameter was infiltrated with solution of quinacrine hydrochloride. Two injections, 1 and 2 cc, were given at weekly intervals. The second injection caused an intense local inflammatory reaction and caused the lesion to ulcerate. Infiltration with quinacrine solution did not affect favorably the course of the disease. It caused early ulceration, irritated the sore, enlarged it and left a big scar about 45 mm in diameter.

EXPERIMENT V-78—A one hundred and fifty-seven day old artificially induced nonulcerated oriental sore, about 15 mm in diameter, was infiltrated with 1 cc of a 10 per cent solution of quinacrine hydrochloride. A week later a second dose of 1 cc was injected locally. Though the first injection seemed to have caused a slight improvement in the appearance of the sore, the second injection was followed by much local swelling which subsided in three days, leaving an ulcerated sore. Because of the intense local reaction, no further injections were given. Quinacrine did not favorably affect the course of the disease, it caused early ulceration. The sore healed by granulation and left a large scar about 35 mm in diameter.

EXPERIMENT V-79—A one hundred and fifty-seven day old artificially produced oriental sore, nonulcerated and about 12 mm in diameter, was infiltrated with 1 cc of a 10 per cent solution of quinacrine hydrochloride. A week later a second dose and one week later a third dose of 2 cc of the solution were injected locally. The third injection caused a severe local reaction with swelling. No further injections were given. The sore did not ulcerate until two months later. It healed just about a year after the inoculation. Infiltration with quinacrine did not influence favorably the course of the disease.

EXPERIMENT V-80—A one hundred and fifty-seven day old artificially produced ulcerated oriental sore was

infiltrated with 2 cc of a 10 per cent solution of quinacrine hydrochloride. A week later a second dose of 2 cc of the solution was injected. The lesion appeared clean and stopped oozing pus. A week later a third injection of 2 cc of the solution was given, which caused severe swelling at the site of the injection, and the ulcer began to grow larger. Fifteen months after the appearance of the sore, it had healed completely and had left a scar about 30 mm in diameter. Infiltration with quinacrine did not affect favorably the course of the disease in this case.

#### CONCLUSION

Six volunteers with oriental sore were treated by infiltrating the sores with a 10 per cent solution of quinacrine hydrochloride. All sores were one hundred and fifty-seven days old. One to three doses of 1 to 2 cc of the solution were injected at weekly intervals. The injections did not favorably affect the course of the disease. My observations essentially confirm those of Marchionini. On the other hand, I have observed that intramuscular or intravenous injections of diethylamine paraaminophenylstibinate<sup>6</sup> (twelve biweekly injections of 5 cc) administered during the ulcerative stage of the sores hastened the process of healing, thus confirming the observations of Dostrowsky<sup>7</sup> (1929). I have also noted that subcutaneous injections of vaccine made with killed *L. tropica* (3,000,000 to 5,000,000 leishmanias per cubic centimeter given in 0.1 to 0.5 cc doses at biweekly intervals) in the pre-ulcerative stage of the sores induced early ulceration and favored the speedy healing of the sores (Ray<sup>8</sup> 1935).

6 The preparation used was neostibosan.

7 Dostrowsky, A. Zur Behandlung der Leishmaniosis cutanea, Arch f Schiffs- u Tropen-Hyg 33 417-423, 1929.

8 Ray, J. C. Studies on Protozoal Vaccine I. Oriental Sore Vaccine, Indian J. Pediat 2 149-158, 1935.



# IMPETIGO BULLOSA IN THE TROPICS

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Impetigo bullosa is one of the dermatologic entities frequently encountered in the tropics. Standard textbooks on dermatology do not convey an adequate description of this disease. Furthermore, previously suggested treatment is not satisfactory. Management of this disease as manifested in the armed forces in the tropics. The purpose of this paper is to present a practical morphologic description of the disease and an adequate method for its treatment.

## INCIDENCE

Of 3,061 men that I examined recently in a survey of the division, impetigo bullosa was present in 32, or 0.7 per cent. The infantry had five times as many cases as the artillery and fifteen times as many as the special troops. It

*Incidence of Impetigo Bullosa Correlated with That of Two Other Cutaneous Diseases in Tropic Troops*

|                | Total<br>Number<br>Examined | Impetigo<br>Bullosa | Per Cent with |                        |
|----------------|-----------------------------|---------------------|---------------|------------------------|
|                |                             |                     | Miliaria      | Impetigo<br>Contagiosa |
| Infantry       | 1,721                       | 1.6                 | 5.4           | 0.2                    |
| Artillery      | 675                         | 0.3                 | 0.9           | 0.4                    |
| Special troops | 665                         | 0.1                 | 1.0           | 0.5                    |
| Total          | 3,061                       | 0.7                 | 2.6           | 0.3                    |

is important to note that the incidence of impetigo bullosa paralleled that of miliaria. Furthermore, the incidence rate of impetigo bullosa had no relationship to that of impetigo contagiosa. The rates are compared in the table.

## HOSPITAL ADMISSION

Patients with impetigo bullosa constituted 0.44 per cent of all patients (898) admitted to the nearby evacuation hospital during November and 3.2 per cent of all those with cutaneous diseases (125) admitted during the same period.

## ETIOLOGY

The organism commonly associated with the disease is a staphylococcus. However, in the survey reported here other organisms were also found microscopically. It was not possible to make any cultures because there were no laboratory facilities available for the purpose.

The most important factor in impetigo bullosa is perspiration. It cannot be overemphasized. The excessive sweating macerates the normal skin and allows bacteria to gain entrance to the superficial portions of the epidermis. Hence it is readily apparent that the lesions occur in the areas of the body where sweating is most profuse, particularly in the hairy regions and where the cutaneous surfaces come into apposition. It is to be noted that in these regions the skin is thin and has less mechanical resistance.

## CHARACTERISTICS

As commonly seen, this disease is characterized by bullous lesions, varying in size from that of a pinhead to that of a dime, arising on the normal skin and surrounded by an erythematous halo. In practically all the cases the disease has an acute onset. The lesions develop rapidly and reach their maturity in less than twenty-four hours. Many new lesions continue to develop daily while the case is under observation.

Impetigo bullosa occurs frequently in the axillae and groins and on the trunk and extremities. It is less common on the face.

The vesicles and bullae vary in elevation from being slightly raised to being well elevated above the normal skin. As a rule they are all sharply demarcated, and each lesion is separate from the other. Coalescence is not frequent. The vesicles and bullae are thin walled and filled with a thin lactescent fluid semipurulent in nature. The contents of the lesions are often easily visible through the semitranslucent wall. Newer lesions and those which have recently reached maturity have a stretched wall, while older lesions have a flaccid wrinkled appearance. The fluid is at first watery and within a few hours becomes cloudy. The demarcation between the watery and lactescent fluid can frequently be seen in the individual bullae through the intact wall. The lesions are fragile and easily ruptured by friction or by contact with clothing. They present a moist glistening surface. The walls of the ruptured bullae rapidly shrink to the outer edges of the lesion and soon form a thin, dry crust. Some patients recover without treatment, but in the majority of cases new lesions continue to develop over a long period.

## TREATMENT

*Prophylactic* Personal hygiene is important in preventing the disease. All factors that will minimize or control perspiration will help in prevention, such as frequent bathing, showers, frequent changes of clothing and frequent use of dusting powder on hairy regions and regions where cutaneous surfaces come into apposition. The clothing worn in the tropics should be of light weight and porous.

Such prophylactic measures are particularly important in units that are engaged in manual labor, because of the difficulty in controlling the deleterious effects of excessive perspiration in such troops.

*Active* It cannot be overemphasized that ointments tend to aggravate the eruption. The commonly advised ammoniated mercury ointments are definitely contraindicated, as they tend to macerate the skin further. It has been my experience that the best treatment is to open the lesions, with aseptic precautions, and allow the fluid to drain out. After this, a 2 per cent aqueous solution of gentian violet medicinal or a drying lotion, such as calamine or magnesium carbonate shake lotions, can be used. Dusting powders containing magnesium carbonate, boric acid and purified talc should also be used to keep the lesions dry. I have also found 5 per cent sulfadiazine jelly to be useful. New lesions

should be opened daily and the surrounding areas kept clean with the use of soap and water. The treatment should be persistent until all lesions are definitely healed.

## SUMMARY

Impetigo bullosa is one of the more common dermatologic entities found among troops in the tropics, particularly in the infantry. The eruption appeared in 0.7 per cent of all troops observed. Most patients with impetigo bullosa were treated in their units satisfactorily. They constituted 0.41 per cent of all admissions and 3.2 per cent of those hospitalized for cutaneous diseases. The most important factor involved in this disease is perspiration. Although it is less frequent, the incidence rate of impetigo bullosa parallels that of miliaria, because the same factors help produce both eruptions. Impetigo bullosa as found in the tropics should be removed from the classification of the impetigo contagiosa group. It is a clinical entity, and sweat is the all-important factor.

The most important part of treatment is prophylaxis. Proper personal hygiene is essential. The commanding officer of the unit has a definite function in prevention and much will depend on him particularly in infantry troops or other troops that do heavy manual labor. Clothing made of light porous material with a coarse weave is recommended for the use of troops in the tropics.

## Obituaries

RALPH HOPKINS, M D

1876 1945

On March 7 there died in New Orleans a distinguished colleague and a friend of long standing. He had known the nature of his mortal illness since the previous autumn, but in his determined way neither his industry in his pro-

his weekly visit to Carville. Four years before, he had retired from his active teaching duties at Tulane, and, missing the stimulating contact with his students, he had redoubled his work in practice and study.



RALPH HOPKINS, M D

1876 1945

essional work nor his consuming interest in his work among the lepers abated the least. Up until a few weeks before his death he led his usual calm and well ordered life, keeping what appointments he could and not failing to make

Ralph Hopkins represented the interesting mixture of Scottish English and French blood. His father, Aristide Hopkins, a cotton broker and ex-Confederate officer, was one of the few men in the combined families not a physician.

His mother, Mary McNeil, came from a well known family most of whose men were in medicine. His early preparatory school work was done in the Dyer School in New Orleans, and his college was that of the Hopkins' family Georgetown. Here he graduated, after a broad classical course, in 1895, with an A B degree. He then entered the Medical Department of the Tulane University of Louisiana and was graduated in 1899. His primary interest was physiology, and his first appointment was as instructor in that department in 1901. Early association with Dr Isadore Dyer precipitated an additional interest in dermatology through the circumstance of an appointment as attending physician to the Louisiana State Leper's Home, now the National Leprosarium at Carville, in 1901. This single association was to last forty-four years, or until the time of his death.

After a term of graduate study at the New York Post-Graduate Medical School and Hospital he became Chief of Clinic and assistant clinical instructor in diseases of the skin at Tulane in 1905. During the next twenty years he maintained a dual connection with the school, becoming assistant professor of physiology in 1917, assistant professor of diseases of the skin in 1921 and then associate professor of physiology, on his appointment as associate professor of dermatology, in 1924, he resigned from the department of physiology. During these years he was closely associated with the clinics of the New Orleans hospitals, notably Charity Hospital. In 1926, after the retirement of Dr Henry Menage, he became professor and head of the department at both Tulane and Charity.

He was commissioned a captain in the Medical Corps of the Army in January 1918 and, after being stationed at Camp Jackson, Miss., went overseas with the Thirty-First Engineers. He remained in France months after the Armistice, engaged in important liaison work, for

which his facility with the language and his ability to deal with the French made him invaluable. On his return he resumed his teaching, his practice and his activity which he valued most, his work among the lepers at Carville.

He was married at Biloxi, Miss., on Aug 11, 1909, to Marian Gayle Denegre and became the father of three sons and three daughters. The home life of the Hopkins was always one of close association and meant much to him, he had already given up the yachting of his younger years and, with the exception of his membership in his single club, preferred to spend his leisure with his growing family. By nature he was distinctly social and hospitable, although his manner was diffident and retiring. Those who attended the meetings held in New Orleans in 1932 and 1941 will have cause to remember him as a gracious and charming host.

In addition to his memberships in the local parish and state societies he had been president of the Louisiana State Dermatological Society and vice president of the American Dermatological Association. He was also a member of the Southern Medical Association and the American Society of Tropical Medicine. He had served as editor of the *New Orleans Medical and Surgical Journal*. In his later years he dropped most of his local club memberships, retaining only that in the Boston Club of New Orleans where it was his unfailing custom to lunch daily. His publications were about equally divided between physiology and dermatology, and of the latter the greatest number were concerned with leprosy. Scientifically Dr Hopkins will long be remembered for his forty-five years of active association with and interest in leprosy for his pioneering in the use of chaulmoogra oil in treatment and his investigations in lepra fever.

R L G

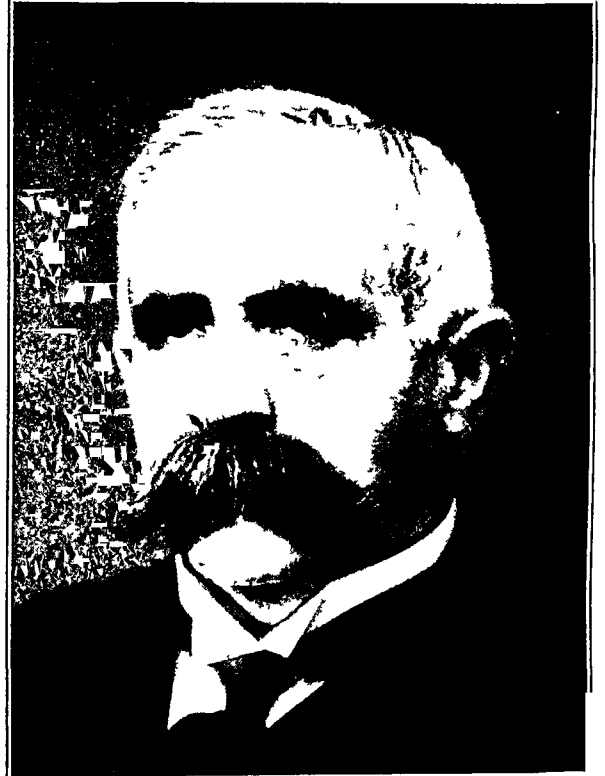
ABRAHAM BUSCHKE, M D  
1868-1943

We have learned with deep sorrow that Abraham Buschke, a dermatologist of unusual gifts and brilliant ideas, died two years ago in Theresienstadt (Czechoslovakia). His wife, his faithful companion of many years, was released from that vast concentration camp and permitted to enter Switzerland a few weeks ago. She brought news of his death.

Abraham Buschke was born in Nakel (Posen) and studied medicine in Breslau, Berlin and Greifswald. It was here, in 1894, that he and Busse described the first case of European blastomycosis (cryptococcosis or torulosis). From that time dated his great interest in mycology. In 1895 he became assistant at Neisser's clinic in Breslau, and in 1897, at Lesser's clinic in Berlin. In 1900 he was appointed instructor in dermatology at the Friedrich Wilhelm University, Berlin, in 1908 he received the title of professor. In 1904 he was made chief of the dermatologic department of the Hospital am Urban (Berlin), and in 1906 he assumed the same position at the Virchow Hospital (Berlin) which he held until 1933. In 1937, when he visited the United States, he impressed many dermatologists in New York with his strong personality and his independent way of thinking.

Utilizing the immense dermatologic material (four hundred beds for dermatologic patients) at his disposal, he almost overwhelmed students in class with all phases and aspects of the subject under discussion. A great number of papers on dermatologic problems were published by him alone or in collaboration with his assistants. Many of these papers dealt with the significance of the skin for immunity in syphilis (1929, with A. Joseph and with B. Peiser) and with the influence of arsphenamine on this immunity. He was a keen observer and described new dermatologic entities, such as scleredema adutorum (1902), keratoderma maculosa disseminata symmetrica (1910, with H. Fischer) and dermatofibrosis lenticularis disseminata (1928 with Helen Ollendorff). Many years before Cicero advocated the use of thallium for tinea capitis, Buschke had studied the effect of thallium on rats. Social aspects of venereal disease, especially in children, were discussed by him and

M. Gumpert. He did not stay within the narrow concept of orthodox dermatology but sought help for the solution of perplexing skin problems in other fields, such as anthropology and chemistry. Even homeopathy came in for some share of his attention when he (in 1921, with Freymann, and in 1923, with Sklarz) tried to explain lichenoid arsphenamine dermatitis as



ABRAHAM BUSCHKE, M D  
1868-1943

caused by the same agent which would cause lichen planus.

His assistants loved his great vitality, although it was not always easy for them to work on to his satisfaction dermatologic problems which he handed them in the morning in the form of cryptic notes scribbled down during the night.

Besides his widow three sons survive him: Franz Buschke, M.D., Albrecht Buschke and William Buschke, M.D. All three reside in the United States.

WILLIAM CURTH, M.D., and  
HELEN O. CURTH, M.D.

# ERYTHEMA NODOSUM IN THE EIGHTEENTH CENTURY

## The Case of the Child Mozart

To the Editor —The belief has often been voiced that Wolfgang Amadeus Mozart (1756-1791), one of the greatest musical geniuses of all times, suffered from tuberculosis of the lungs. This opinion is based on such meager evidence as the belief of one of his first biographers, G. N. von Niessen,<sup>1</sup> who married Mozart's young widow, or on the vaguely noted observations that Mozart was a sickly child, that he often suffered from colds and catarrh and that he was always tired and close to exhaustion.<sup>2</sup> The cause of his early death, according to the death certificate, was "miliary fever." However, according to a medical expert of the early nineteenth century, it was "meningitis,"<sup>2b</sup> and according to J. Barraud,<sup>3</sup> who in the early twentieth century collected all the data available on the symptoms and signs of Mozart's last illness it was Bright's disease. The story that Mozart died from meningitis was built up in defense of Salieri, the composer's great enemy, who was more or less openly accused of having poisoned Mozart. But it seems highly improbable that meningitis was the cause of Mozart's death, because he did not lose consciousness until shortly before death, according to the statements of several eyewitnesses.<sup>2b</sup> More than that, he stopped work on his "Requiem" only four hours before he died.<sup>2b</sup> Hence, one cannot decide, on the basis of available data, whether or not Mozart ever suffered from tuberculosis or from what disease he died.

It is interesting to note, in any case, that the child Mozart had a typical attack of erythema nodosum when he was 6 years 9 months old. This diagnosis is deduced from a detailed description of that disease by his father, Leopold Mozart, titular court composer of the archbishop's orchestra in Salzburg, Austria. The illness occurred during the second concert tour made by the Mozart family. The party included the father, the mother and the two children. The trip began Sept. 18, 1762. The weather was rainy and windy all the time. Because of the interruptions of travel, it took two and a half weeks for the family to go from Salzburg to Vienna. In Linz, Wolfgang had "catarrh." But otherwise, "in spite of all irregularities and in spite of rain and wind, he remained healthy, thank God" (letter of L. Mozart to L. Hagenauer, Vienna, Oct. 16, 1762).<sup>4</sup> Five days after this report by Mozart's father and after Wolfgang was introduced with great success at the Imperial Court of the Empress Maria Theresa, the child suddenly became sick.

The letter in which Leopold Mozart describes his son's disease was dated Vienna, Oct. 30, 1762, and was addressed to his landlord and friend, Lorenz Hagenauer,

to whom he faithfully reported all the great and small events of the concert tour. The English translation reprinted here is in great part copied from Emily Anderson's excellent book.<sup>5</sup> I have deviated from her translation in a few places where I felt that a more literal interpretation might be advantageous in considering Mozart's medical history. In part, the letter reads: "Many a slip between cup and lip. I was beginning to think that for 14 days in succession we were far too happy. God has sent us a small cross, and we must thank His infinite goodness that things have turned out as they have. At 7 o'clock in the evening of the 21st we again went to Her Majesty, the Empress.

"Our Woferl, however, was not quite as well as usual, and before we drove there and later when he went to bed he complained of his—I beg your pardon—'buttocks and hips.' When he got into bed, I examined the places where he said he had pain and found several spots as large as a kreutzer,<sup>6</sup> very red and slightly raised and painful to touch. These spots were present only on the shins, on both elbows and a few of them on the buttocks, altogether, they were very few. He was feverish, and we gave him black powder<sup>7</sup> and a margrave powder<sup>8</sup> but he had a rather restless night. On Friday we repeated the powders both morning and evening and we found that the spots had spread but although they were larger, they had not increased in number. We had to send messages to all the nobles, with whom we had engagements for the next eight days, and had to cancel them day after day. We continued to give margrave powders, and on Sunday Woferl began to perspire, as we wanted him to, for hitherto his fever had been rather dry. I met the physician of the Countess von Zinzendorf (who happened to be out of town) and gave him particulars. He at once came back with me and approved of what we had done. He said it was a kind of scarlet fever rash.

"Thank God, he is now so well that we hope that if not to-morrow, his nameday, at least on the day after to-morrow he will get up for the first time. Meanwhile this affair has cost me fifty ducats at least.<sup>9</sup>

But I am infinitely grateful to God that it has turned out so well. These scarlet fever spots which are a fashionable complaint for children in Vienna, are dangerous and I hope that Woferl has now become acclimatised. I beg you to use every effort to ascertain what His Grace<sup>10</sup> will do eventually and what hopes I may entertain of the post of Vice-Kapellmeister."

5 Anderson, E. 'The Letters of Mozart and His Family,' New York, The Macmillan Company, 1938, vol. 1, p. 12.

6 A coin of penny size.

7 Pulvis epilepticus niger, a common remedy at that time against all kinds of disorders (footnote of E. Anderson<sup>5</sup>).

8 A remedy discovered by the German chemist Andreas Sigismund Markgraf, 1709-1782 (footnote of E. Anderson<sup>5</sup>).

9 The income lost by performances the child prodigy was unable to give.

10 The Archbishop of Salzburg, Hieronymus Count of Colloredo (1732-1812).

1 von Niessen, G. N. Biographie W. A. Mozarts, Leipzig, Breitkopf and Hartel, 1828.

2 (a) Jahn, O. W. A. Mozart, ed. 3, Leipzig, Breitkopf and Hartel, 1891, vol. 2, pp. 637-647. (b) Schurig, A. Wolfgang Amadeus Mozart, Leipzig, Breitkopf and Hartel, 1923, vol. 2, pp. 371-379.

3 Barraud, J. A quelle maladie a succombe Mozart? Chron. med. 12 737, 1905.

4 Schurig,<sup>2b</sup> vol. 1, p. 115.

As one can see Leopold Mozart, a greedy and pedantic little man, gave a precise and careful description of his son's disease. The sudden onset and short duration of the eruption, the exclusive localization of the red raised spots on shins, buttocks and elbows and the tenderness of the lesions are so characteristic of erythema nodosum that the reader, if he happens to be a twentieth century dermatologist, will hardly have any doubt about what the correct diagnosis should have been. One finds it intriguing also to note that the high ranking physician to whom Leopold Mozart felt very much obligated<sup>11</sup> misdiagnosed this eruption as "a kind of scarlet fever rash." But nobody should blame him for not having diagnosed erythema nodosum, as this syndrome was first mentioned in medical literature forty-six years later in Robert Willan's famous classification of cutaneous diseases.<sup>12</sup>

Those who agree with Wallgren,<sup>13</sup> Feer,<sup>14</sup> Kundratitz<sup>15</sup> and other pediatricians that erythema nodosum in small children always represents a manifestation of the generalization phase of tuberculosis may conclude that Wolfgang Amadeus Mozart went through this phase of tuberculosis when he was not yet 7 years old.

STEPHEN ROTHMAN, M.D. Chicago

University of Chicago

### IMMUNIZATION THERAPY OF WARTS

To the Editor.—In reply to the letter of Brigadier G. M. Findlay, kindly forwarded to me on May 23, 1945, I should like to make the following remarks:

1 As I clearly stated in my paper, I referred to Dr. Findlay's publication, relying on the citations of it by Dr. Rulison in his paper (*ARCH DERMAT & SYPH* 46:66 [July] 1942). The latter wrote (p. 77) "Findlay stated that warts of one species are not transferable to another and that their extracts have no curative effect in different species." If there is a misrepresentation in my paper, I should be excused to a certain degree, in view of the fact that the statement attributed by Dr. Rulison to Dr. Findlay in 1942 had been left uncontested until now. Nevertheless I can only express my regret for not having consulted the original before.

2 However, Rulison's interpretation of Findlay's statements becomes understandable, even if we quote directly from Dr. Findlay's monograph (Findlay, G. M., in Andrewes, F. W., Arkwright, J. A., and others: *A System of Bacteriology in Relation to Medicine*, Medical Research Council, London, His Majesty's Stationery Office, 1930, vol. 7, p. 252). On page 257 of the original text are found the following statements: "Serra (1924)

11 His professional fee, rather splendid, was a concert given by Wolfgang in the doctor's home. (Letter of L. Mozart to L. Hagenauer, Vienna, Nov. 6, 1762, reported by Schurig,<sup>b</sup> vol. 1, p. 119.)

12 Willan, R. *On Cutaneous Diseases*, London, J. Johnson, 1808, vol. 1.

13 Wallgren, A. *Considerations sur l'erytheme nouveau*, *Acta paediat* 5:225, 1926.

14 Feer, E. *Zur Aetiologie des Erythema nodosum*, *Schweiz med Wchnschr* 56:682, 1926.

15 Kundratitz, K. *Zur Frage der Aetiologie des Erythema nodosum*, *Jahrb f Kinderh* 113:155, 1926.

was unable to infect laboratory animals with human warts. Ullmann (1923) claims to have produced a papilloma in the vagina of a bitch by inoculation with laryngeal papilloma. The writer has been unable to confirm these results. Dog warts failed to infect man, rabbits, mice and guinea pigs, as did bovine warts. Human warts were not infective for dogs, rabbits, rats, mice or guinea pigs." In his letter Dr. Findlay refers to this as follows: "At the time this was written, this was a fair summary of the position, since the experiments of Frank Schultz (1908) are entirely uncritical." Thus he confirms rather than refutes Dr. Rulison's interpretation of his statements and results.

3 With regard to the second part of Rulison's quotation I concede that Findlay did not mention that he had used a vaccine. However, he used an immune serum, the results of which point in the direction of the same conclusions which Dr. Rulison ascribed to Dr. Findlay, whom I now quote (p. 257): "The writer found that after inoculating himself with three crops of warts, he became immune to further inoculations. The serum, however, had no antiviral properties, but after hyperimmunization acquired them. Dogs are also capable of producing an antiviral wart serum, but serum which acts on human warts has no action on dog warts and vice versa." This shows that even though Dr. Findlay did not express an opinion about specific active immunization he expressed an opinion about passive immunization to the effect that an immune serum for warts of one species did not act on warts of another species. This may explain the remark by Dr. Rulison who erroneously referred to an extract instead of an immune serum.

4 I disagree with Dr. Findlay when he calls the publication of Frank Schultz (*Deutsche med Wchnschr* 34:423, 1908) "entirely uncritical." This, in my opinion, is an unjustified criticism. Schultz's article gives well selected literary references and (with minute details) the description of an experiment made with material from cattle warts by J. Jadassohn on 3 of his assistants, 1 of whom was Frank Schultz. The warts which developed at the sites of inoculation were described in detail, both clinically and histologically. This experiment (in addition to several clinical observations) is more decisive as to whether warts are transferable from one species to another than many negative results, such as Dr. Findlay's and my own. Therefore, I cannot agree with Dr. Findlay's summary of the situation at the time (1930) that his paper was written.

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### CORRECTION

In the abstract of "A Case for Diagnosis (Acquired Localized Trichorrhesis, [Trichoclasia], Keratosis Pilaris?) by Dr. Francesco Ronchese, presented before the New England Dermatological Society at its Feb. 9, 1944 meeting, which appears in the June 1945 issue of the *ARCHIVES (ARCH DERMAT & SYPH)* 51:412, 1945), the last line of the legend for the illustration on page 413 should read 'wavy epidermis, hyperkeratosis, indentations and absence of atrophy, of coil and sebaceous glands'."

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

NEVUS FLAMMEUS ASSOCIATED WITH CONJUNCTIVAL TELANGIECTASIA AND POSSIBLE EARLY CHOROIDAL TUMOR EMANUEL ROSEN, *Am J Ophth* **27** 1143 (Oct) 1944

The author reports on a nevus flammeus involving the left side of the face and neck. Besides these cutaneous regions of vascular involvement, there was telangiectasia of the left side of the palate and posterior tonsillar wall. The lower lid exhibited a conjunctival structure that was extremely red, and the bulbar conjunctiva had an increased formation of tortuous and racemose vessels. A small white plaque just above the disk was seen on ocular examination.

In the discussion the author points out that a nevus of the face apparently involves the first two branches of the trigeminal nerve and that any structure supplied by this nerve may be involved. The object of the report was to stress the clinical importance of nevi and telangiectases so that patients may be referred to the proper specialist, by whom the presence of nevus anemia, familial combined hemangioma of the cerebellum and retina and hemangiomas may be detected.

STRAKOSCH, Denver

POLYARTICULAR ARTHRITIS AND OSTEOMYELITIS DUE TO GRANULOMA INGUINALE J LYFORD III, R B SCOTT and R W JOHNSON JR, *Am J Syph, Gonorr & Ven Dis* **28** 588 (Sept) 1944

Three patients with polyarticular arthritis and osteomyelitis caused by granuloma inguinale are reported on by Lyford, Scott and Johnson. In the first patient there occurred a systemic dissemination of the disease with massive polyarticular arthritis and ultimately ulceration of many of the joints and a widespread destruction of the bones. In the second patient there was involvement of two vertebrae and a hip joint, communicating with sinus tracts presenting in the inguinal region. In the third patient lesions developed in the bones of a hand and forearm but no involvement of the joints was observed.

The course of disease in these patients adds further proof that granuloma inguinale can be a systemic as well as a local disease. No satisfactory explanation for the mode of spread of the Donovan bodies within the host could be given in these instances, but the massive involvement of the bones and joints in 1 patient suggest that the spread could be hematogenous.

The fact that no member of any of these patients' families had granuloma inguinale suggests that infection involves more than mere contact with material from an active lesion.

REUTER, Milwaukee

EFFECT OF 3,4-BENZOPYRENE ON REGENERATING EPIDERMIS OF MICE MARTIN SILBERBERG and RUTH SILBERBERG, *Arch Path* **38** 215 (Oct) 1944

Silberberg and Silberberg report on experimental studies which showed that benzene applied to regenerating epidermis of mice accelerated healing of wounds and that the migration of cells into the defect along

with intensification of proliferation was hastened. When benzopyrene in benzene was applied in a similar manner, the epithelization of the wounds was not hastened to the same extent as the proliferation of the cells. While cells were abundant, they failed to migrate into the defect at a rate commensurate with their increased multiplication.

THE RELATION OF CHEMICAL STRUCTURE IN CATECHOL COMPOUNDS AND DERIVATIVES TO POISON IVY HYPERSENSITIVENESS IN MAN AS SHOWN BY THE PATCH TEST HARRY KEIL, DAVID WASSERMAN and CHARLES R DAWSON, *J Exper Med* **80** 275 (Oct) 1944

In a previous study Keil corroborated the experimental work of Landsteiner and Jacobs demonstrating a relation between the cutaneous response to poison ivy extract and 3-geranyl catechol. In this report Keil, Wasserman and Dawson present evidence based on patch tests in support of the view that the active ingredient in poison ivy is a catechol derivative with a long, unsaturated side chain in the 3 position. The position of the side chain in the catechol configuration has some bearing on the degree and incidence of group reactions in persons hypersensitive to poison ivy. The group reactions discussed in this paper relate only to those resulting from the various catechol and veratrol compounds. Preliminary studies by the authors indicate that this sensitiveness extends to other phenolic derivatives.

LYNCH, St Paul

THE PRINCIPLES OF PERCUTANEOUS ABSORPTION STEPHEN ROTHMAN, *J Lab & Clin Med* **28** 1305 (Aug) 1943

This review covers the literature of the years from 1920 to 1942. From the available data the following conclusions were drawn.

Overton's rule, which postulates that lipid-soluble substances enter the living cells and that lipid-insoluble substances do not is largely valid as far as percutaneous absorption is concerned. The impermeability of the skin to water and electrolytes is caused neither by the presence of a greasy or waxy cover of the skin nor by the presence of the horny layer. The barrier to absorption is to be found in the transitional layers between cornified and noncornified epithelium, in the stratum granulosum and the stratum lucidum, which represent an electric double layer with positive hydrogen ions on the outside and negative hydroxyl ions on the inside. The presence of appendages in the skin complicates the mechanism of percutaneous absorption mainly because any substance may penetrate into the follicular canal and reach the duct of the sebaceous glands and from there the gland cells, thus avoiding the passage through a stratified epithelium and directly contacting cells whose permeability is higher than that of the granular layer of the epidermis. If there is any absorption of lipid-insoluble electrolytes, the route is through the appendages. Ointments are helpful in bringing the incorporated substances closer to the sur-



face of absorbing cells, this task is the more easily performed the more supple the ointment is. However, there is no evidence that either ointments or any other kind of "vehicle" may serve as a transportation vehicle into the cell itself. Choosing a substance to which the skin is completely impermeable, one will be unable to enforce absorption with any kind of ointment. Lipid solvents, however, such as ether and chloroform, enhance the permeability of the skin by disintegrating the lipid frame of the cells and thus create nonphysiologic conditions. Similarly, saponins, which precipitate the cholesterol, will break up the barrier to cutaneous absorption.

With the use of galvanic current to introduce substances into the skin under the usual conditions of medical electrophoresis, the absorption through appendages will be tremendously increased but the impermeability of the epidermis will remain unchanged. Under extreme conditions the electrophoretically introduced substances will penetrate through the follicular wall sideways and enter the epidermal cells from there, but the surface epithelium will not be broken through.

ROTHMAN, Chicago

COTTON HOSE AS A VEHICLE FOR A FUNGICIDE IN TREATMENT OF ATHLETE'S FOOT. PHOEBE J. CRITTENDEN and LUELLA S. JOINER, *J. Lab. & Clin. Med.* **29** 606 (June) 1944

This is a report on a preliminary study of the treatment of dermatophytosis, the results of which were promising. The duration of infection varied from a few days to twenty or more years. The good results reported in the treatment of fungous infection of hands and feet with copper sulfate administered iontophoresis led the authors to the idea of impregnating cotton hose with the fungicide, since it brought the fungicide into close contact with the feet while walking and with the shoe lining, which is a frequent source of reinfection.

The authors noted that a 5 per cent solution of copper sulfate reduced the effect of the fungi, but it proved to be irritating to the skin in warm weather. Copper acetate was found to be less irritating than copper sulfate and was substituted for it in treatment of patients not responding satisfactorily to the latter. The itching was usually relieved within a week. The shoes were not damaged.

The hose were changed daily. The soiled hose were soaked in tap water at 70 C for thirty minutes. They were then washed in soap suds, rinsed and dried. The clean dry hose were soaked for thirty minutes in a 5 per cent solution of copper at 40 C and then wrung through an ordinary clothes wringer set loosely but giving enough pressure so that the solution was evenly spread throughout the hose without dripping.

THE ADJUVANT EFFECT OF AEROSOL UPON THE GERMICIDAL ACTION OF CADMIUM CHLORIDE. ARTHUR F. COCA, *J. Lab. & Clin. Med.* **29** 689 (July) 1944

In his experiments to demonstrate the enhancement of fungicidal action of a fungicidal agent through the admixture of an adjuvant, the investigator used a proved germicide, cadmium chloride, and a well known wetting agent, aerosol OT (sodium dioctyl sulfosuccinate). In making these selections the following pertinent factors were considered: 1. The fungicidal agent should be one of relatively low toxicity and nonirritative to the cu-

taneous tissues. 2. It should be able to penetrate into cutaneous tissues and into infective fungi. If the agent itself does not possess the property of diffusion, a non-irritative adjuvant should be added. 3. The agent or mixture must be applied in such a manner as to allow it sufficient time for effective penetration of infective tissues and fungi.

The results showed that cadmium chloride alone in concentrations of 0.5 and 0.25 per cent in 20 per cent alcohol was incapable of sterilizing suspensions of the micro-organism used in the tests, whereas the aerosol in the same solvent failed to kill micro-organisms in concentrations of 0.0625 per cent. The same two concentrations of cadmium chloride did sterilize the suspension when mixed with the aerosol in concentrations as weak as 1:256 and 1:64 respectively. The experiments were performed with a constant quantity of well shaken suspension of *Monilia albicans* filtered through a silk fabric.

GELBER, Los Angeles

ROLE OF INOSITOL IN ALOPECIA OF RATS FED SULFASULIDINE. EDWARD NIELSEN and A. BLACK, *Proc. Soc. Exper. Biol. & Med.* **55** 14 (Jan) 1944

Inositol, 5 mg six days weekly, succeeded in curing rats of alopecia produced by the administration of sulfasulidine in addition to a synthetic diet believed to be complete nutritionally. From the beginning of the time inositol was incorporated in the diet, the growth was better, and the fur coat was smooth, with normal luster.

EXPERIMENTS ON THE TOXICITY OF THE CALCIUM SALT OF PENICILLIN. PAUL GYORGY and P. C. ELMES, *Proc. Soc. Exper. Biol. & Med.* **55** 76 (Jan) 1944

Freeze-dried calcium salts of penicillin were found to be no more toxic to mice than the sodium salt of penicillin. The dose employed in some of these experiments was approximately fifty times as great in proportion to body weight as the daily dose of sodium salt used at present in human therapeutics. No toxic signs developed when the calcium salts were administered to a human subject. The authors conclude that satisfactorily purified calcium salt of penicillin is not more toxic to human beings or mice than its sodium salt.

HANSEN, Galveston, Texas  
[AM. J. DIS. CHILD.]

DISTURBANCES OF VISUAL ADAPTATION AND THEIR CLINICAL SIGNIFICANCE. CHARLES SHEARD, H. P. WAGENER and L. A. BRUNSTING, *Proc. Staff Meet., Mayo Clin.* **19** 525 (Nov. 1) 1944

In the skin vitamin A is concerned with the process of keratinization. In conditions caused by long-standing deficiency of vitamin A the skin becomes dry and hyperkeratotic. These changes are evident microscopically as follicular hyperkeratosis, parakeratosis and dyskeratosis. In some patients with keratosis pilaris and in some with certain rare familial dyskeratotic diseases of the skin, such as pityriasis rubra pilaris and keratosis follicularis, there is collateral evidence of a disturbance of the metabolism of vitamin A.

In the study of patients with cutaneous diseases possibly associated with a disturbance in the metabolism of vitamin A, there are three approaches to be made to accurate diagnosis, namely, (1) measurement of the threshold of dark adaptation, (2) measurement of the

level and the tolerance curve of vitamin A in the blood and the feces and (3) estimation of clinical response to therapy consisting in the ingestion or injection of vitamin A

TROPICAL ANIDROTIC ASTHENIA STUART D. ALLEN and J. P. O'BRIEN, M. J. Australia 2 335 (Sept 23) 1944

Tropical anhidrotic asthenia is a clinical syndrome observed in tropical areas among troops who have suffered from malaria rubra and is characterized by anhidrosis, changes in the skin and enlargement of the axillary and the inguinal lymph nodes, with symptoms of exhaustion occurring in the heat. Complete recovery usually takes place in six to twelve weeks.

Characteristic cutaneous changes are present. On the forehead and face sweating may be profuse. The palms and soles and perhaps the axillas are normally moist. But for these exceptions the body is completely devoid of sweat and the skin is perfectly dry. On the trunk and the extremities the skin is coarser than normal. On close inspection the affected skin is seen to be studded with innumerable grayish white papule-like elevations about 1 mm in diameter. When one of the elevations is pricked with a needle, a minute drop of watery fluid may be obtained.

On the basis of histologic study of the abnormal skin it is considered that occluding hyperkeratosis surrounding the sweat duct as it emerges on the surface of the stratum corneum is responsible for this syndrome. The hyperkeratosis is a result of previously occurring malaria rubra.

HENSCHEL, Denver

OBSERVATION OF SKIN DISEASES IN THE TROPICS JAMES R. DELANEY, U. S. Nav. M. Bull. 42 1117 (May) 1944

Cutaneous lesions among personnel engaged in battle operations in the South Pacific were common enough to result in the loss of an enormous number of man hours.

Fungous infections, the most common type of disease, involved 80 per cent of all personnel and varied from mild dermatophytosis to secondarily infected dermatophytid. Malaria, which affected the second largest number of men, varied from mild localized lesions to involvement of almost the entire cutaneous surface. Ulcers of the skin, which occurred frequently, were located on the lower extremities and were caused by trauma, infection, contact or allergy or a combination of such factors. Irritation from soap was also common, owing to the inability to remove the soap because of the scarcity of bathing facilities.

YAWS HAROLD A. LYONS, U. S. Nav. M. Bull. 42 1168 (May) 1944

Yaws is rare in the white race, nevertheless, an increased incidence may be expected as a result of contact precipitated by the present war.

The author reports a case in which the disease was contracted by a medical officer on duty in a native clinic for the treatment of yaws on one of the Solomon Islands. The initial lesion started at the site of an insect bite on the finger, followed shortly afterward by a maculopapular eruption on the trunk. Dark field examination revealed spirochetes resembling *Treponema*

pertenue, and a Kahn test of the blood gave a 4 plus reaction. Healing was rapid after a course of treatments with a bismuth compound.

COCCIDIOIDOMYCOSIS PAUL MICHAEL, RICHARD F. McLAUGHLIN and PHILLIP L. CENAC, U. S. Nav. M. Bull. 43 122 (July) 1944

The authors report a case of coccidioidomycosis with a latent period of seven years unsuccessfully treated with 3,081,000 units of penicillin, administered both intravenously and intrathecally. Sulfadiazine administered for six days in adequate dosage also failed to produce any improvement in the patient's condition.

ROBIN, South Bend, Ind.

IMPETIGO CONTAGIOSA CURED BY FEVER OSCAR GREEN, U. S. Nav. M. Bull. 43 136 (July) 1944

Impetigo contagiosa involving the lips healed in five days following a temperature of 104.2 F during an attack of malaria. Natural or induced fever, the author suggests, may be of possible therapeutic value for this disease.

ACTION OF ELECTRIC BLANKETS G. MALCOLM BROWN and K. MENDELSSOHN, Brit. M. J. 1 390 (March 18) 1944

The electric blanket has advantages which recommend it for certain clinical conditions. It is safe and causes no discomfort at ordinary heating rates. There is less risk of burns than with the radiant-heat cradle, and little supervision is required. It occupies little space and is almost fool proof. The most important disadvantages are the long delay before maximum temperature is reached and the lack of variability of control. The electric blanket acts by conduction of heat to the patient. It raises the body temperature only half as quickly as the radiant heat cradle, even when the bed is previously warmed.

SHAW, Chattanooga, Tenn.

PHEMERIDE A NEW ANTISEPTIC DETERGENT C. N. ILAND, Lancet 1 49 (Jan. 8) 1944

Phemeride (parateritaryoctylphenyldiethoxybenzyl-dimethyl ammonium chloride) probably acts as an antiseptic by disrupting or interfering with the functions of the bacterial cell membrane.

The material was obtained as a white powder without odor which dissolved readily in water and alcohol. A small series of clinical tests were made. Laboratory and clinical tests suggested that phemeride is inhibitory to the common pathogens in dilutions not toxic to the tissues.

LANGMANN, New York [Am. J. Dis. Child.]

HERPETIC STOMATITIS IN INFANTS AND CHILDREN T. F. McNAIR SCOTT, Proc. Roy. Soc. Med. 37 310 (May) 1944

There is a common stomatitis occurring among infants and young children that has been called by many names, such as aphthous, membranous, ulcerative or Vincent's stomatitis. The disease is due to a primary infection with the virus of herpes simplex and hence can be called herpetic stomatitis. The clinical picture of the disease is as follows. It attacks children be-

tween the ages of 1 and 6 years, the onset is sudden, with fever (the temperature may reach 105 F), anorexia and general malaise. It lasts from seven to fourteen days. The local manifestations are as follows: 1. The gums are red and spongy. 2. Shallow, yellowish, painful ulcers appear on the tongue and buccal mucous membranes as a result of ruptured vesicles. 3. The regional lymph nodes are enlarged. 4. There is a marked oral factor. There are two main types of the disease, primary and recurrent. Complications consist of (1) dehydration, (2) impetiginization of accompanying labial herpes and (3) paronychia in thumb suckers. Tests are described in the article to show the herpetic etiology of the condition. Treatment is entirely palliative.

WILLIAMSON, New Orleans  
[AM J DIS CHILD]

PERIARTERITIS NODOSA OF KUSSMAUL AND MAIER. E. GALAN and M. PEREZ-STABLE, Bol Soc cubana de pediat **15** 635 (Oct) 1943.

This is an extensive and careful review of the whole subject of periarteritis nodosa. The authors state that they are describing in another bulletin the first case of this disease in a child to be reported from Cuba. They review the literature in detail, point out the different etiologic theories and in many instances give tabular summaries of the work reported by other authors since Kussmaul and Maier's original contribution, in 1866. They discuss the pathologic anatomy, the clinical signs and symptoms, the prognosis, the diagnosis and what little treatment has been recommended. They bring the subject up to date, in 1943, and make this an excellent reference article for any one interested in the details of the subject.

KEITH, Rochester, Minn  
[AM J DIS CHILD]

## ATLANTIC DERMATOLOGIC CONFERENCE

JOSEPH KENNEDY, M D, *Chairman*

HAYDEN KIRBY-SMITH, M D, *Secretary*

Feb 26, 1944

**Erythema Perstans** Presented by LIEUT COMDR  
E E BARKSDALE (MC), USNR

Miss B F E, white, aged 20, complained of itching, burning red spots. Six years ago, while she was taking high school freshman examinations, red, itching, burning lesions appeared, one on her right hand, one on her right thigh and one on her right buttock. At the same time she had similar sensations on her left eyelid but noted no discoloration of the skin. The lesions lasted about one week and then faded, leaving dark brown scaly macules where the erythema had been.

Since that time the patient has had ten to twelve such attacks. At first they were spaced about a year and a half apart and appeared only at times of mental stress (she had an attack when her father died), she has had two attacks in the last six weeks and does not consider that she has been under any nervous strain in this time.

The longest attack lasted about eight days, while the shortest was four days. Between attacks the affected areas maintain the same coffee-colored, scaly appearance. The left eyelid has never shown any discoloration, but the conjunctiva becomes mildly injected during the period of symptoms.

The menstrual history is regular, with a twenty-six day interval and a five day duration with moderate cramping. There is no noticeable relation between her cutaneous symptoms and her menstruation.

### DISCUSSION

DR D M SIDLICK, Philadelphia. According to the patient's statement, the flat, circumscribed, purplish colored lesion on the dorsum of the hand is not the only lesion she has had. There have been other lesions on other parts of the body. Also, according to her statement, the lesions are of a more or less evanescent character. Some have disappeared completely. In others, like the lesion on the dorsum of the hand, the inflammatory reactions have become less intense at times and have then been followed by an acute exacerbation. To a query regarding constipation she answered "No," but on occasion she does take a laxative of the nature of Ex-Lax. I believe that this is a dermatitis medicamentosa caused by phenolphthalein.

DR EUGENE F TRAUB, New York. The patient presented several localized areas of erythema, with some scaling and pigmentation. The lesions were scattered—one on the hand, another on the thigh and I believe, on the eyelids—and they always remained at these definite sites. The story is that at various times the eruption flares up and then subsides. This is certainly the history of a fixed erythema, and I believe this patient has a drug eruption, though it may not necessarily be phenolphthalein that is responsible. Frequently fixed drug eruptions are caused

by chemicals other than phenolphthalein, and even occasionally a fixed drug eruption may flare up from one of several different offenders.

DR SAMUEL M PECK, Bethesda, Md. Dr Chargin has pointed out a number of facts in his paper on fixed drug eruptions due to arsenic which are of interest. I had the privilege of examining the histologic sections of his cases. The clinical appearance of the lesions could not be differentiated from that of a fixed eruption due to phenolphthalein. Histologically, they were seen to consist of two primary changes. The changes in the epidermis consisted of hyperpigmentation, and the changes in the cutis consisted of vascular dilatation, plus chromatophoric pigment as well as free pigment in the cutis, especially around the blood vessels. These histologic changes account for the color of a fixed eruption, namely, subepidermic pigment plus the dilated vessels being responsible for the bluish brown appearance. The persistence of the discoloration is due to the pigment in the cutis and not to blood pigments, as is commonly supposed.

DR FRED WEIDMAN, Philadelphia. It does not suffice simply to secure the history regarding phenolphthalein taken as a purgative. The drug may also be ingested in ices of cakes and candies which have been made pink by phenolphthalein.

LIEUT COMDR E E BARKSDALE (MC), USNR. This is thought to be a fixed drug eruption. We have not definitely been able to diagnose it from the history of the patient. However, she admits that she has taken Ex-Lax tablets.

NOTE—Since this case was presented, she was given ½ grain (0.03 Gm) of phenolphthalein by mouth, which produced a definite exacerbation of the eruption in a few hours.

**A Case for Diagnosis (Kaposi's Sarcoma, Lichen Planus Hypertrophicus?)** Presented by MAJOR  
Z N KORTH, MC, AUS

D N, a 28 year old white woman of German-English extraction was seen on Feb 25, 1944 in the outpatient department of the Walter Reed General Hospital. The history is as follows. In August 1941 swelling, stiffness and pain in the joints of the hands developed. Involvement in other joints, including the shoulders and knees, followed. Periapical infection was found in 1943, which led to the extraction of all lower teeth and clearing of all articular symptoms.

In January 1942 there developed a "lump beneath the skin" about the size of a "marble." It was situated on the right calf and was painful and tender. Within a month the area had become bluish and was of the diameter of an orange, although the area remained rather flat. At about this time the area broke down, draining a yellowish watery material. Wet packs and rest for about one month brought about healing, leaving only a thickened, bluish and rather firm area. Some time later, just after one of the patient's visits to the hospital for biopsy, lesions developed on the elbows in the same fashion as was previously related. These lesions increased to their present size and have remained almost stationary for several months. They are, however, tender, and

slight trauma to them causes considerable swelling and tenderness. About April 1943, swelling in the lower extremities became noticeable, and shortly after this, painful bluish nodules began to form on the distal portion of the legs. Since then there have been gradual extension and increase in the size of the lesions until at present the distal half of the leg is almost completely involved.

No laboratory investigation has been made, since the patient was first seen only twenty-four hours ago. Four biopsies have been done in the past, but in no instance has the patient been told anything of the results.

Examination revealed numerous nodules varying from 0.5 cm. in diameter to large plaque-like areas involving the distal half of both lower extremities.



Kaposi's sarcoma? Lichen planus hypertrophicus? (Army Medical School negative 3655-1)

On the upper half of the legs there are several nodules in different stages of development. One, a comparatively recent lesion, is apparently situated deep in the cutis, is firm and tender to palpation and has an erythematous area above it. Other lesions are deeply violaceous, scaly and indurated and slightly tender. Many show mild to severe degrees of atrophy. The large plaque-like lesions on the distal portion of the legs show numerous changes, including atrophy, small ulcerations, pinpoint hemorrhages, lichenification and scaling. There are papular areas which on close examination are deeply violaceous, some superficially and some deeply situated, which appear to be dilated vessels and petechiae. To the outer side of the midline on either leg in the middle third there is a board-like area of induration entirely separate from any of

the lesions previously described and above which the skin appears to be normal.

*Past History*—The patient had kidney trouble when 7 years old and the usual childhood diseases.

*Biopsy* (Report submitted by Dr. Fred Weidman subsequent to the meeting)—Obviously, the tissue reaction is of the most acute leukocytic type and is accompanied with profound degeneration and inflammation of the blood vessels. This suggests the presence of a hematogenous disease of the order of that which occurs in erythema elevatum diutinum or, less likely, periarteritis nodosa. In relation to the clinical appearances, the absence of pigmentation is noteworthy and indicates, no doubt, the selection of an early lesion for biopsy. It seems inconceivable that such a degree of leukocytic infiltration as is seen here and as much infiltration as was seen clinically could be exhibited in purpura annularis telangiectodes. Certainly the microscopic picture is not that of Kaposi's sarcoma. All things considered, clinically and histologically the disease should be regarded for the time being as of unestablished diagnosis pending additional biopsy of the major lesion. It is conceivable that bromides or iodides could produce such a reaction, but the histologic picture is not diagnostic of such.

*Pathologic Diagnosis*—The diagnosis was acute, diffuse, presuppurative dermatitis (like erythema elevatum diutinum).

#### DISCUSSION

DR JACOB H. SWARTZ, Boston. I should like to add the diagnosis of lupus vulgaris. The color is suggestive of it.

DR FRED WEIDMAN, Philadelphia. Kaposi's sarcoma appears to be the most likely diagnosis to me. The lesion is woody, hard and deep brown, and an occasional small superficial hemorrhagic bleb appears here and there. Moreover, several "satellite" lesions well above the major one are almost purely hemorrhagic. I grant that the lesion is much more sharply circumscribed than is usual for Kaposi's sarcoma.

DR MAURICE J. STRAUSS, New Haven, Conn. I do not have a diagnosis to offer, but none of the diagnoses which have been suggested explain the scleroderma-like induration of the subcutaneous tissues and muscles in the region involved. These indurations may or may not be connected with the lesions, but I think that they should be taken into consideration.

DR EUGENE F. TRAUB, New York. It seems to me that Kaposi's sarcoma could be excluded as a diagnostic possibility in this case on clinical grounds alone. In the first place, the sex and nationality do not favor the diagnosis, and unless these lesions have been desiccated or treated with some strong chemicals, causing this peculiar scarring and healing, Kaposi's sarcoma would not look like this, according to my experience. Overlying what seems to be pigmented hypertrophic scar tissue are what appear to be hemorrhagic vessels. While vessels or blisters can occur in Kaposi's sarcoma, such occurrence is very rare. Frequently there is a peculiar verrucous formation on the toes, such as is often seen in cases of elephantiasis, which is entirely lacking in this patient and which is generally present in Kaposi's sarcoma. Despite the history, I should still further consider the possibility that this is an eruption due to either an iodide or a bromide. This could account for all the changes seen in the patient.

DR LEON GINSBURG, Baltimore. I suggest the possibility of scleroderma-like sarcoid.

### Lichen Planus Atrophicus Presented by DR FRANK J EICHENLAUB, Washington

Mrs S A C, a white woman 48 years old, reports that an eruption first appeared about one year ago on the sides, front and back of the neck and has developed gradually since then. The only medical factor of importance in the case is that she has had hyperthyroidism, which was treated with roentgen ray therapy two years ago.

On the front, sides and back of the neck there are shiny, white, scaly, angulated and in places umbilicated papules, some discrete and some confluent.

The eruption on the back of the neck has improved with roentgen ray therapy and with injections of a bismuth compound.

#### DISCUSSION

DR FRANCIS A ELLIS, Baltimore. Five years ago at the Atlantic Dermatologic Conference in Baltimore, several patients were shown with this disease, and Dr H Montgomery (*ARCH DERM & SYPH* 42 755, [Nov] 1940) corrected the diagnosis and differentiated lichen sclerosus et atrophicus from atrophic lichen planus. The clinical and pathologic picture is pathognomonic and is similar to that of kraurosis vulvae.

DR BERNARD APPEL, Lynn, Mass. I have always been interested in the controversy over the nomenclature of this disease—whether it is lichen planus atrophicus et sclerosus or lichen sclerosus atrophicus and whether the “planus” is left in or not. Several years ago my view was more or less clarified because I had the opportunity to study a patient who showed a classic picture of lichen planus with the purple, flat, polygonal, pruritic papules typical of a textbook description. In close association, also, were numerous larger, oval, sharply outlined, white, waxy, atrophic areas, such as this patient has shown today. The controversy on nomenclature will undoubtedly continue, but in my opinion this patient today shows evidence of lichen planus as well as of lichen sclerosus et atrophicus.

DR REUBEN GOODMAN, Washington, D C. Lichen planus or not, the end result is the same. The histologic structure shows practically little difference.

CAPT RICHARD L SUTTON JR, MC, A U S. I like the name, “white spot disease,” that Wise and Rosen used (*J Cutan Dis* 35 66, 1917). It does not have the prognosis, I believe, that lichen planus does, one would not expect a patient with such a disease to have violaceous papules on the wrists or the lumbosacral region.

DR FRANK J EICHENLAUB, Washington, D C. When I presented this patient, I had hoped to present 2 other patients with similar eruptions. This patient was presented with a diagnosis of lichen planus atrophicus. The other 2 patients had what clinically was lichen sclerosus et atrophicus, 1 being the patient whose case was published by Montgomery under that diagnosis. All 3 of these patients improved from roentgen ray therapy and injections of a bismuth compound. One must conclude, therefore, either that lichen sclerosus is in fact a variation of lichen planus or that it does respond to the same type of treatment, a conclusion which is contrary to that of Montgomery's reports.

DR BERNARD APPEL, Lynn, Mass. Apropos of the statement of a previous speaker of a preference for the name of “white spot disease,” it seems to me that use of that name would be a step backward and not a progressive one. One of the most important

contributions dermatologists could make would be to agree on the nomenclature. I am sure that in the “Standard Nomenclature of Disease” there is no disease called “white spot disease.” Furthermore, such an indefinite term could well be applied to many dermatologic entities and, I believe, would only be confusing. If dermatologists try to follow the standard classification in the “Standard Nomenclature of Disease” they will be taking a definite step toward crystallizing thought about the clinical pictures involved.

### Peculiar Alopecia Symptomatica Presented by DR FRANK J EICHENLAUB, Washington

Miss N L B, a white woman 19 years old, reports that six years ago she had a severe attack of influenza with a high fever. After this, most of her hair fell out. When it grew in again, it grew normally on the sides and back but not on the top and front, where it never grew to more than an inch or so in length. She was treated by a dermatologist, with no beneficial results at that time. Her basal metabolic rate was said to have been normal.

I first saw the patient on Oct 27, 1943. Then, as now, her hair was normal and healthy at the back and sides of the scalp but short on the top and front, in the usual “bald area” of men.

Microscopic examination of both the short and the long hairs showed nothing abnormal. Her basal metabolic rate on Nov 20, 1943 was —26 per cent on the first test and —22 per cent on the second.

The alopecia has not materially improved with local treatment and thyroid extract by mouth.

#### DISCUSSION

DR ELMER R GROSS, Wilmington, Del. I wish to suggest a diagnosis of trichotillomania. This patient has absence of the pharyngeal reflex and of the corneal reflex, which places her disease in a category of psychosomatic dermatology, namely, that of a compulsion neurosis.

DR MAURICE J COSTELLO, New York. The half-dollar-sized area of partial baldness with broken off but healthy looking hairs is due, I believe, to mechanical injury to the hair and the scalp, caused by the friction of vigorous rubbing with ointments and a hair brush by the patient and her mother in an effort to stimulate growth of hair.

### Necrobiosis Lipoidica Diabeticorum Presented by DR RUSSELL J FIELDS, Washington, D C

Mrs R M C, a white woman, presents a lesion on the anterior surface of each foot of about two years' duration, with the lesion on the left foot appearing first. She has had diabetes for five years. When the lesions were originally discovered, her weight was 150 pounds [68 Kg], and it came down to 96 pounds [43.5 Kg]. The lesions itch moderately, and there is also some burning and aching.

She presents a yellowish red lesion the size of a half-dollar on the anterior aspect of the left foot. It is subject to changes of color.

#### DISCUSSION

DR FRED WEIDMAN, Philadelphia. While I agree with the diagnosis of necrobiosis, there are, nevertheless, some hard, gritty nodules a short distance below the lesion, these made me think of an alternative

diagnosis of calcinosis cutis A biopsy of the nodules is well worth while

**Paraffinoma** Presented by DR H F ANDERSON and DR CAROLINE BURPEAU, Washington, D C

Mrs J H R, a white woman aged 34, first noticed a mass in her left arm on July 31, 1942, which has been gradually growing since then The lesion appeared while she was having a course of injections of estrone in oil

She presents a hard, indurated, slightly tender red mass, irregular in outline Biopsy of a specimen taken on Sept 16, 1942 revealed a typical Swiss cheese appearance deep in the cutis The usual cellular elements were lacking and there was no foreign body giant cell reaction

In January 1943, even though no further injections had been given a new nodule appeared The lesion from which the specimen for biopsy was taken has never completely healed and from it bits of a substance resembling paraffin are removed from time to time I am presenting the patient in order to receive advice as to further therapy

#### DISCUSSION

DR FRANCIS A ELLIS, Baltimore I suggest the diagnosis of sesame oil tumor A report of a patient with a tumor due to this agent was presented by Dr Conrad (*J A M A* 121 237 [Jan 23] 1943) at the Ninety-Second Annual Meeting of the American Medical Association, at Atlantic City, N J, in 1942 Histologically, sesame oil tumors have less of the "Swiss cheese" appearance than this tumor has The fat globules are more uniform, and there is less foreign body reaction The only satisfactory treatment is excision of the tumor

DR MAURICE J COSTELLO, New York I had under my observation a patient in whom a systemic reaction developed after each injection of estrone in oil (2,000 U S P units) The manufacturers suggested that the reaction might be caused by the vehicle, oil of anise, and not by the estrone itself An intradermal test with 0.05 cc of the oil caused an erythematous reaction When this subsided, a pea-sized nodule (paraffinoma) remained for months I agree with the diagnosis offered by Dr Anderson

DR EUGENE F TRAUB, New York Formerly persons were given injections of various types of oil not only for medicinal purposes but for cosmetic purposes The sites where injections were given for cosmetic purposes on the face often became lumpy in a relatively short time, but frequently tumors did not develop for as long as ten to fifteen years afterward I believe that the only type of treatment which is satisfactory in such cases is complete excision of the tumor mass

DR FRED WEIDMAN, Philadelphia In my experience with experimental paraffin tumors in monkeys, metastasis to regional lymph nodes took place, accordingly, I favor the excision of this patient's lesion

DR LLOYD W KETRON, Baltimore I cannot quite understand the histologic structure of this lesion There is a broad area of necrosis in the deeper portion of the section with practically no foreign body reaction

DR HARRY F ANDERSON, Washington, D C I thought that this patient was interesting enough to be presented because some of the nodules developed two or three months after the oil had been injected into her arm Paraffinoma and sesame oil tumors are identical entities from the histologic standpoint

**Acute Disseminated Lupus Erythematosus** Presented by DR HAYDEN KIRBY-SMITH, Washington, D C

T C, a white girl, in the spring of 1940 began to have an acute eruption involving the face, the hands and the feet She was seen by a dermatologist and given four injections of a gold preparation, after which her eruption became worse She was hospitalized for six weeks, during which time she received four blood transfusions of  $\frac{1}{2}$  pint (237 cc) each and nicotinamide She improved and continued to take nicotinamide for three months She had complete remission of the eruption until the spring of 1941, when she had a slight recurrence, with lesions in the mouth She was given 15 cc of liver intramuscularly twice a week, compresses of a solution of aluminum acetate were applied to the hands and the feet, and the lesions in the mouth were treated with silver nitrate These treatments were continued until the early summer of 1942

The attack had completely subsided and the patient was apparently well until January 1943, at which time she had a recurrence, preceded by rheumatic pains She was seen by another dermatologist and was hospitalized for three weeks, during which time she was given four blood transfusions of 1 pint (473 cc) each and nicotinic acid daily There was no improvement and the patient returned home in a critical condition During the various attacks the temperature varied from 99 to 104 F

The patient was first seen by me in July 1943, presenting brownish pigmentation, dryness and crusting of the entire face and scalp and complete alopecia of the scalp She also had edematous, oozing erythematous patches involving the terminal phalanges of the hands and feet She appeared to be acutely ill, with a temperature of 104.8 F

Treatment consisted of daily injections of 1 cc of liver extract intramuscularly, a preparation of vitamin B complex, a proprietary preparation of fresh liver, iron and copper daily and transfusions of 500 cc of citrated blood given every other week She gave a history of being sensitive to sulfanilamide and to sulfathiazole She was given 2 tablets (1 Gm) of sulfadiazine every four hours In forty-eight hours her temperature rose to 106 F Use of sulfadiazine was stopped, and from then on the patient slowly improved, the temperature gradually receded to normal, and by the end of October the patient was able to get out of bed During her illness her weight dropped from 105 pounds (47.6 Kg) to 73 pounds (33.1 Kg) The Wassermann and Kahn reaction of her blood were negative During the acute illness, the white cell count went down to 4,000 and the red cell count to 2,400,000

#### DISCUSSION

COMDR L K MACCLATCHIE (MC), U S N R I saw this patient in her first attack First she had a discoid type of eruption Three or four injections of a gold preparation were given, the dose gradually being increased to a maximum of 15 mg After an initial improvement, symptoms of intolerance developed and the use of the gold preparation was discontinued Shortly after this a subacute disseminated type of eruption appeared on the palms and soles, in the mouth, under the nails and on the trunk and extremities Also the patient lost her hair There was a suspicion of lesions of the bladder, as cystitis developed which her general physician was unable to explain Treatment of the cystitis with sulfonamide compounds given orally was tried, and it was hoped that there might be some



effect on the lupus, as there were infected tonsil tags. The patient, however, was intolerant to sulfonamide compounds as well as to any other drugs tried. It was finally necessary to hospitalize her, and she was given blood transfusions, vitamins by mouth and injections of nicotinamide. After discharge from the hospital, she was given injections of liver. On this regimen the patient had a complete remission of symptoms, and she went back to work. It is interesting to note that she has had three severe attacks, the last one apparently being an acute disseminated lupus erythematosus.

DR JACOB H SWARTZ, Boston. I want to stress the importance, from my own experience, of the focus of infection in cases of acute disseminated lupus erythematosus which begin with a discoid type of eruption. I recall a girl recently who had two attacks. In 1 instance an abscessed tooth was found. After it was removed, she first became worse and then recovered completely. Six months later she had another similar attack, coincidental with a peritonsillar abscess. A second recovery, with clearance of the focus, followed. Of course, that is only 1 instance. I think that the focus of infection is something to consider seriously, especially in cases in which the disease starts with a discoid type of eruption that later becomes disseminated. One must also differentiate this type of the disease from that of the acute disseminated lupus erythematosus, which begins as such. The prognosis of the latter is much more unfavorable.

DR BERNARD APPEL, Lynn, Mass. I should like to make a few remarks about the use of gold preparations. I am still in that apparently fast-disappearing group who continue to use gold for the discoid type of lupus erythematosus. I should like to make a statement and an inquiry. It seems to me that the form of gold which was first introduced by Dr Obermayer a number of years ago, gold sodium succinimide, is a useful salt of gold. I have had some interesting experience with its use for 2 patients who were extremely sensitive to gold sodium thiosulfate. One was so sensitive that after she had been given 5 mg she displayed a rather severe reaction. I was able subsequently to give these 2 patients as high as 200 mg of gold sodium succinimide, with no untoward effect. I have continued the use of that particular drug in a number of cases with I believe, fairly good clinical result. I have not had opportunity to buy any recently, and I do not know whether or not it is still available. The query I should like to make is: Has any one else used that particular drug, and what is his experience with it?

DR MAURICE J STRAUSS, New Haven, Conn. Several years ago I had 2 patients with lupus erythematosus in whom severe reactions developed when they were treated with gold sodium thiosulfate. Perhaps Dr Appel will recall that at that time he suggested to me that I try gold sodium succinimide in treating these patients. He even gave me the name of the chemist who could supply the material. I used this for both patients, and both patients had as severe reactions as they did when gold sodium thiosulfate was used. I still have 2 Gm of gold sodium succinimide in my possession, which I shall be very happy to give to Dr Appel.

DR SAMUEL M PFCK, Bethesda, Md. I think that one should be cautious in the terminology one uses in cases of lupus erythematosus, because of the prognosis attached to the type of lupus erythematosus designated. Acute lupus erythematosus has a bad prognosis and almost invariably leads to death. The disease which is designated as chronic discoid lupus erythematosus, even when it is generalized or a superimposed acute lupus

erythematosus develops, has a better prognosis. The papers of Klemperer and Baehr have shown that in cases of acute lupus erythematosus one is dealing with a generalized vascular disease, and histologically there are vascular changes which are characteristic of it. Such changes are demonstrable in lesions of the kidney post mortem but are occasionally observed in the cutaneous lesions. I have also been able to point out that the snake venom test always elicits a positive reaction in the patient with true acute lupus erythematosus even when the disease is in the early stage, with lesions first appearing on the face and before they have become widely disseminated, but in the discoid type there never is a positive reaction. In patients with a negative reaction the disease, even when it resembles the acute type, has a better prognosis than in those with a positive reaction. I have had favorable results with Germanin in cases of the chronic discoid type. The dose was usually 20 to 30 mg given once a week. With such doses renal complications were avoided.

DR MAURICE J COSTELLO, New York. Soon after Dr Peck and his associates treated patients who had the fixed type of lupus erythematosus with injections of Germanin given intramuscularly, we hospitalized 4 patients with the discoid type of this dermatosis, which had been resistant to the conventional therapy. One patient who had had an extensive discoid type of the disease was completely cured and had no complications from the drug. Although the others were greatly improved, the administration of Germanin had to be discontinued because of severe toxic reactions, including renal damage and toxic dermatitis. I have used naphuride sodium (the preparation manufactured in the United States under the trade name of Naphuride Winthrop) in treatment of the fixed type of lupus erythematosus without success.

DR HARRY F ANDERSON, Washington, D C. The patient at the present time, in all likelihood, is in a period of remission. I was caring for her about six months ago, at which time there were casts in her urine and articular pains. Her cutaneous manifestations were severe, and she looked as though she were about at the end of the road. There was no favorable reaction to blood transfusions and the administration of liver extract, after many other methods of procedure had failed. I am glad to see her looking so well today and wish to compliment Dr Kirby-Smith.

#### Epithelioma, Probably Arising From Sweat Glands. Presented by DR H F ANDERSON, Washington, D C.

E S, a white woman, aged 74, received a bump on the head while in an automobile. Soon after that she noticed a swelling developing on the top of her head. The tumor remained for about three years, with gradual increase, before she consulted me, on Jan 4, 1944.

The tumor mass consisted of grouped nodules, rounded, hard, waxy and nonulcerating. The whole group covered an area of about 4.5 cm in diameter. At the time of examination this group of nodules were the only ones noticed. Later three discrete lesions were found in the scalp, some distance away from the original group.

Biopsy showed definite epithelioma, very cellular. The cells in some areas assume formations resembling glandular arrangement.

The treatment to date has consisted of the administration of a total of 2,500 r of roentgen radiation through a 1 mm aluminum filter plus wide electrocoagulation to all areas.



## DISCUSSION

DR HARRY F ANDERSON, Washington, D C This patient has been presenting new lesions at a rapid rate. In the last three weeks three distinct nodules as large as 1 cm in diameter have developed. The diagnosis is undoubtedly the turban type of epithelioma.

**A Case for Diagnosis (Rosacea-Like Tuberculid of Lewandowsky, Rosacea?)** Presented by MAJOR MURRY M ROBINSON, MC, A U S

L E is a woman aged 51 years. Her family history shows that one brother was cured of pulmonary tuberculosis.

The lesions first appeared in 1938. Since then they have been present at all times. There has been no remission, although there has been some variation in the number and severity of the lesions.

There are discrete lesions on the face, forehead and temples. They are erythematous with a slight brownish hue, varying in size from that of a pinhead to that of a split pea. They are papular and papulopustular in character. The surrounding skin is hyperemic. On diascopic examination the lesions have a yellowish brown color. Their centers are somewhat soft. A toothpick can be inserted with ease and is retained in position.

The result of a tuberculin test was negative after seventy-two hours. A roentgenogram of the chest showed no evidence of tuberculosis.

Microscopically the section studied showed a small nodule, over which there was some thinning of the stratified layer. Below this there was some eosinophilic degeneration of the collagen. The nodule itself was inflammatory, with considerable round cell infiltration. There was considerable proliferation of endothelial cells and formation of giant cells.

DR SAMUEL M PECK, Bethesda, Md. The physician's clinical description and the histology seem characteristic of tuberculosis miliaris faciei. In favor of such a diagnosis is the fact that the lesions tend to clear up spontaneously. The reaction to the tuberculin test is negative in about 50 per cent of patients with tuberculosis miliaris with concentrations of tuberculin as high as 1:100. The tuberculin patch test is not as reliable as the intradermal test, since it does not give a qualitative result, which is important in this instance.

DR MAURICE J STRAUSS, New Haven, Conn. I believe that a definite diagnosis of rosacea-like tuberculid should not be made in this case. It is my recollection that in such cases there usually is an increased sensitivity to tuberculin. Apparently the opposite is true in this case.

**A Case for Diagnosis (Squamous Cell Epithelioma?)** Presented by DR LAWRENCE McCaleb, Washington, D C

A D L, a woman aged 22, has a lesion which started one and a half years ago and has been spreading. It is located in the inner canthus of the right eye. The right side of the bridge of the nose is indented. The lesion is pea-sized and has crusted borders with pearly edges.

## DISCUSSION

DR EUGENE F TRAUB, New York. The duration of the lesion, in my opinion, practically excludes the possibility of its being a squamous cell carcinoma. Coupling this with the clinical appearance, I believe that a diagnosis of basal cell epithelioma is inevitable. A

slow-growing, rather firm, nodular lesion in this location that has given rise to practically no subjective symptoms is almost invariably a basal cell lesion. I should expect a squamous cell lesion to reach the size of the present growth within a few weeks, and it would have characteristics that would be entirely different from those of the present lesion.

DR FRED WEIDMAN, Philadelphia. I should like to submit the diagnosis of healed dacryocystitis. Although the lesion is more conspicuous on one side, the eruption is bilateral. The deep, narrow depression suggests a previously existing sinus rather than the healed ulceration of a cancer. The patient's statement that time and again tears course down over her cheeks suggests an obstruction of the lachrymal duct. A nonpathogenic thread organism, *Actinomyces foersteri*, sometimes produces large colonies in the duct, becomes calcified and results in the formation of a calculus. This obstructs the duct and, as the result of a secondary infection, there is a communication with the cutaneous surface by the formation of a sinus.

**Mycosis Fungoides, Tumor Stage** Presented by DR HAYDEN KIRBY-SMITH, Washington, D C

J L B, a white woman aged 33, has had a generalized eruption of thirteen years' duration. She was first seen at Georgetown University Hospital, complaining of severe itching. She presented at that time well defined excoriated lichenified patches. Her disease was diagnosed as a chronic eczematoid dermatitis, and she improved greatly with fractional doses of roentgen rays.

She was first seen by me in 1941, presenting well defined, grouped, erythematous, infiltrated, thickened, excoriated patches, especially about the face, extremities, chest and back. A specimen was taken for microscopic examination. This patient has been treated by means of antipruritic lotions, solution of potassium arsenite and subfractional doses of roentgen rays in order to control the itching. During the past year numerous nodules and tumors have developed which have regressed rapidly with roentgen ray therapy.

The Wassermann and the Kahn reactions were negative. Hematologic examination showed white cells, 6,200, red cells, 4,500,000, polymorphonuclear leukocytes, 76 per cent, lymphocytes, 16 per cent, eosinophils, 6 per cent, and band forms, 2 per cent.

**Scleroderma** Presented by LIEUT COMDR E E BARKSDALE (MC), USNR

A D E, a white youth aged 18, complains of areas of pain and anesthesia of three months' duration. He was in Cuba for eight months prior to transfer here. He was well until about the middle of September 1943, when he began having "sharp, stabbing pains" in the region of the left instep. A few days later he began to have similar pains in the right foot and after about a month he had similar pains in his hands. He cannot describe the pains as being in any certain area in his hands, nor can he say whether they were superficial or deep.

About the time that the symptoms appeared in the hands, the pains disappeared from his feet, being replaced by a numbness of the skin and a "drawing" sensation, the toes being involuntarily flexed. Within a short time the symptoms in his hands showed similar change. Paresthesias of a stocking and glove type became so great that he would burn his fingers with cigarettes. He noticed that he could not completely extend

his fingers and that his hands were so weak that he was continually dropping objects. Atrophy of the interosseus muscles was apparent at this time. Coincidentally with the paresthesia, he noted that the skin over the involved areas was dry and somewhat wrinkled and showed fine scaling. Since the onset, the left hand and the right foot have shown more involvement than the opposite members, but all affected parts have grown gradually worse. He has lost 25 pounds (11.3 Kg) since the onset of his symptoms. His present weight is 110 pounds (50 Kg).

Physical examination showed that both hands are held in a position of partial flexion, the left hand is flexed more than the right, though the right is capable of greater voluntary flexion. Neither hand can be fully extended. The interosseus muscles of the left hand seem to be paralyzed and partially atrophic, while those of the right hand are partially paralyzed and not yet atrophic. The interosseus muscles of the feet show similar changes.

The skin in stocking and glove arrangement over all extremities shows dryness, smoothness to palpation and minute scaling. There is complete absence of the senses of touch, temperature and position in the left hand. The right hand and both feet show these sensations to be diminished though not completely absent.

Roentgenologic examination of both hands revealed no evidence of osseous changes. The basal metabolic rate was +2 per cent. Results of a spinal puncture were negative. The Kahn reaction was negative, the blood count was normal, and urinalysis showed nothing abnormal. Fluoroscopic examination on Dec 10, 1943 showed demineralization of tarsal, metatarsal, carpal and metacarpal bones.

At present the right hand has cleared considerably, there is a suggestion of nerve distribution there now, in that the little finger and the ulnar surface of the ring finger show more involvement than the remainder of the digits. There is an anesthetic area on the right shin about 6 inches (15 cm) long and 3 inches (7.6 cm) wide. Also there are several anesthetic spots on the left shin. These areas of anesthesia are not sharply demarcated but rather show regions of comparative numbness between the spots of complete loss of sensation and the normal areas. There is an area of thickening, slight induration and some scaling on the dorsum of the left forearm.

#### DISCUSSION

LIEUT. COMDR E. E. BARKSDALE (MC), USNR. The question of leprosy in this patient has been brought up. So far no organisms have been found. Biopsy of this boy's skin suggested the possibility of scleroderma.

DR. SAMUEL M. PECK, Bethesda, Md. I hesitate to make a diagnosis of scleroderma in this case. It seems to me that the skin lacks the typical feel of scleroderma. I believe that these are secondary atrophic changes following a nerve injury.

CAPT. RICHARD L. SUTTON JR., MC, AUS. I agree with Dr. Peck that this is not a case of scleroderma. I submit the diagnosis of infectious neuritis.

DR. MURRY M. ROBINSON, Washington, D. C. The only indication that would make it possible to consider the diagnosis of leprosy is the clawhand. I have seen many patients with this disease, and there is nothing about this patient that suggests leprosy to me. In a clawhand of this degree due to leprosy one would expect to see atrophy of the interosseus muscles. In addition, this patient has been in the tropics recently for eight months. I believe that it is an accepted fact that the incubation of leprosy is much longer.

**Parapsoriasis** Presented by DR. FRANK J. EICHENLAUB, Washington, D. C.

The patient is a white man aged 30, with active pulmonary tuberculosis for which he is undergoing treatment at Glenn Dale Sanatorium. He presents an eruption, chiefly on the trunk, of six months' duration. It consists of flat, salmon-colored, scaly macules, from 0.5 to 2 cm in diameter, which do not itch and which have failed to respond to local treatment.

#### DISCUSSION

DR. FRANK J. EICHENLAUB, Washington, D. C. The diagnosis that I made (I did not write the record) was simple macular parapsoriasis.

DR. LOUIS GOLDSTEIN, Philadelphia. I do not agree with the diagnosis as presented, because the patient's dermatitis bears no resemblance to the plaque or the guttate type of parapsoriasis and because his lesions lack the necrosis and scarring which is characteristic of the Habermann variety. Since this patient has advanced active pulmonary tuberculosis, he harbors an infectious focus which is sufficient to cause a cutaneous dissemination of the toxic process as seen in the "id" phenomenon in many an infection. I am therefore inclined to consider his as a nonspecific eruption of tuberculous origin, although from its outward clinical appearance it may not necessarily fit into the localized or hematogenous classification of cutaneous tuberculosis.

**Syringocystadenoma** Presented by DR. FRANK J. EICHENLAUB, Washington.

T. G. S., a white man aged 42, has had an eruption since 1923. He states that the lesions developed gradually over about a year's time and have since remained stationary.

He presents on the front of the trunk about two dozen elevated, hard, smooth, brownish yellow nodules from about 5 to 7 mm in diameter.

Biopsy specimen, presented with the patient, shows the lesions to be made up of benign sweat gland epithelium, looking essentially like normal sweat glands, with a surrounding cellular infiltrate.

#### DISCUSSION

CAPT. RICHARD L. SUTTON JR., MC, AUS. This is an exceptional case in its extensiveness and is of interest and value to the meeting. The patient said his lesions do not swell when he sweats, although some lesions of syringocystadenoma do. The patient of Sutton and Denme (*J. A. M. A.* 58:333 [Feb 3] 1912) showed engorgement of his lesions when pilocarpine was given. The disease is not familial in his case, the patient says.

**Xanthoma Tuberosum** Presented by DR. JOSEPH V. KENNEDY, Washington, D. C.

P. J., a white man aged 22, states that about one and a half years ago an eruption began on the right elbow. It has spread rather slowly but now involves both elbows and both knees. Recently the eruption has spread to the right palm.

Examination reveals the presence of multiple yellowish nodules on the extensor surfaces of the elbows and knees and, to a slight extent, on the palm of the right hand. These lesions show dilated blood vessels on the surface. There are no subjective symptoms.

A roentgenogram of the chest showed the lungs and heart to be normal, and an electrocardiogram was within normal limits. A urinalysis disclosed nothing signifi-

cant The basal metabolic rate was —11 per cent The nonfasting blood sugar level was 140 mg per hundred cubic centimeters, the fasting level, 120 mg The cholesterol level was 246 mg (normal, 140 to 190 mg) per hundred cubic centimeters and the sedimentation rate 2 mm per hour The hemoglobin content was 97 per cent, the red blood cell count, 4,360,000, and the white cell count, 6,000, with 64 per cent polymorphonuclear leukocytes, 28 per cent small lymphocytes, 3 per cent monocytes, 2 per cent eosinophils, 1 per cent basophils and 2 per cent transitional forms

### A Case for Diagnosis (Dyskeratoid Dermatitis?)

Presented by MAJOR Z N KORTH, M C, A U S

F D, a white man aged 24, was admitted to the Walter Reed General Hospital on Feb 21 1944 His complaint was itching over the neck, axillas, groins, perineum and buttocks About April 1, 1943, he noticed "blisters" developing on the right elbow These cleared rather promptly with the use of a lotion Later "reddened" areas began to appear in the axillas, on the back of the neck, in the groins and on the buttocks, which after a few days became vesicular and then crusted There has always been severe pruritus

Examination revealed discrete and confluent erythematous eczematoid patches In the groin particularly and on the medial aspect of the left thigh there is a dollar-sized group of vesicles No lesions are present on the neck, and stroking the area failed to elicit more than a mild erythematous response

The patient's father as a young man had had some form of eruption on his hands which was finally cleared with an undetermined type of radiation treatments A brother had had a vesicular eruption on his hands and arms, which according to the patient, was similar to his own disease but much less severe

Laboratory determinations included red cells, 4,400,000, hemoglobin content, 85 per cent, white cells 8,300, with polymorphonuclear leukocytes, 56 per cent, lymphocytes, 36 per cent, monocytes, 2 per cent, eosinophils, 6 per cent Other observations were not remarkable, excepting those made on the biopsy specimen A slide is presented for examination

### DISCUSSION

DR WALTER F LEVER, Boston I favor the diagnosis of dermatitis herpetiformis, because of the sudden onset of the eruption, the intense itching and the distribution of the lesions The buttocks and the posterior surfaces of the thighs are typical locations for dermatitis herpetiformis I suggest that the patient be given sulfapyridine, and in a few days it will be clear whether or not the diagnosis of dermatitis herpetiformis is correct

DR FRANCIS A ELLIS, Baltimore I agree with the diagnosis of dermatitis herpetiformis Dr M H Goodman claimed that oral lesions can occur in this disease The lesions in the axilla are more infiltrated and elevated than usual Some patients with this disease do not respond to sulfapyridine, even though the concentration in the blood is raised to 18 or 20 mg per hundred cubic centimeters Other patients may remain free of lesions by the ingestion of 1 Gm of sulfapyridine a day

DR WALTER F LEVER, Boston Sulfapyridine has been, in my experience, superior to sulfanilamide Far smaller doses of sulfapyridine are required for the control of the eruption Sulfathiazole was found to be of little value, sulfadiazine and sulfaguandine, of no value

DR JACOB H SWARTZ, Boston I believe that this work has already been completed and reported The results were not comparable with those derived from the use of sulfapyridine

CAPT RICHARD L SUTTON JR, M C, A U S I had a patient with dermatitis herpetiformis and chemo-resistant gonorrhea, course after course of sulfathiazole and sulfadiazine did not help either his gonorrhea or his dermatitis He received no sulfapyridine, however, which, as Dr Costello pointed out—first, I believe—(ARCH DERMAT & SYPH 42 161 [July] 1940), is the most effective of the sulfonamide compounds in the treatment of this dermatosis When my patient received 100,000 units of penicillin, his gonorrhea was cured at once in the usual dramatic fashion but his dermatitis herpetiformis showed no response at all, not even temporary

DR ADOLPH ROSTENBERG, Washington, D C I should not make a diagnosis of Dühring's disease in this case I should like to ask a question concerning the use of sulfapyridine in the treatment of this disease As I recall the report by Swartz and Lever (ARCH DERMAT & SYPH 47 680 [May] 1943), sulfapyridine was found to be the most effective of the sulfonamide drugs, sulfanilamide was of less value, and sulfathiazole, sulfaguandine and sulfadiazine were practically of no value This suggests to me that it may be the pyridine portion of the sulfapyridine molecule which is causing the improvement It is interesting to note that nicotinic acid is pyridine-3-carboxylic acid To carry this hypothetical reasoning one step further, if it is the pyridine which is effective, it may be because there is a deficiency of nicotinic acid for which the pyridine is to some degree compensating I should therefore suggest that nicotinic acid or its amide be tried in the treatment of this disease

### Superficial Benign Basal Cell Epithelioma Presented by DR H F ANDERSON and DR CAROLINE BURPEAU, Washington, D C

A P F, a white man aged 48, has had psoriasis for years His treatment has included both roentgen ray therapy and the administration of arsenicals The eruption diminished, and for many years the patient did not bother about having treatment On Nov 20, 1943, he presented himself to me, complaining of what he thought were new patches of psoriasis These patches were scattered over his chest and neck and had been present for at least a year and a half

On the chest and neck there were sharply defined plaques Scales were extremely fine and adherent These patches also presented eczematoid changes, pigmentation and atrophy

One of the lesions on the neck was removed for biopsy and showed typical superficial benign basal cell epithelioma

### DISCUSSION

DR FRANCIS A ELLIS, Baltimore It is interesting that this patient has psoriasis and that many years ago he took arsenic for several years Some cases of this type have been reported as cases of psoriasis in which malignant degeneration occurred, whereas the patient actually has multiple superficial epitheliomatosis due to the ingestion of arsenic Histologically, this type of epitheliomatosis can be differentiated from other forms by the dyskeratosis and vacuolation of the rete cells

CAPT RICHARD L SUTTON JR, M C, A U S This type of lesion is spoken of as "multicentric" in origin, because the usual section, perpendicular to the skin,

shows neoplastic epithelium adjacent to the epidermis in numerous islets. Madsen, in 1940, reported the examination of such lesions through the use of tangential sections, which revealed that tumor tissue forms a network applied to the under surface of the epidermis as a circumscribed, continuous, retiform, discoid mass of neoplasia (quoted by me in ARCH DERMAT & SYPH 46 37 [July] 1942, from the abstract in Wise, F., and Sulzberger M. B. Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, 1941, p. 494). The "multicentricity" then exists only for those who see ordinary sections. If one looks at the lesion from a distance of 6 feet (1.8 meters) it looks like the solitary lesion that it is.

**Psoriasis, Contact Dermatitis** Presented by DR H. H. HAZEN, Washington, D. C.

The patient began tile work in 1923 and had no trouble until October 1942, when a dermatitis developed on the palms and the backs of the fingers. He stopped tile work in December 1942 and took a clerical job. In March 1943 he was finally referred to another dermatologist, who gave him a patch test for cement and found that he reacted positively at the end of six days. The patient continued with treatment prescribed by this dermatologist until November 1943. While under active treatment, he received roentgen ray therapy. From April to November he used sandpaper and dihydroxyanthranol in benzene. A sulfated fatty acid (Acidolate) was substituted for soap for cleansing purposes.

In November 1943 the patient consulted another dermatologist, whose diagnosis was psoriasis. A biopsy was performed on tissue from the web of the thumb, and the pathologist to whom the tissue was sent reported that the disease was psoriasis. However, careful study of this report and personal examination of a slide show that while the lesion may have been one of psoriasis it was more probably a lichenification or represented a chronic dermatitis following continued irritation. It should be noted that no microabscesses were present and that there was an unusual amount of edema in all layers.

With regard to the diagnosis, it should be noted that psoriasis of the palms alone is exceedingly rare, that there was no erythema present, that the edges were not well defined, that there was no pitting of the finger nails, that there had been no spontaneous improvement of the hands since the trouble first appeared, and that with simple, nonirritant treatment there was improvement within ten days after I first saw him, Jan. 24, 1944.

This case exemplifies the difficulty that sometimes arises in making a diagnosis of industrial dermatitis. The difficulty of making a diagnosis from microscopic observations in cases of certain common diseases is illustrated.

DR SAMUEL M. PECK, Bethesda, Md. The clinical impression is that this is a case of contact dermatitis, possibly due to alkalis or solvents. In the absence of typical psoriatic lesions, I should hesitate to make a diagnosis of psoriasis of the hands or feet.

DR JOHN W. MARTIN, Washington, D. C. I am interested in this case because I was called on to testify before the Employee's Compensation Commissioner of the United States government as to whether this man had contact dermatitis from cement. At that examination there was no resemblance to contact dermatitis; rather, it was characteristic of dermatophytosis, pustular bacterid or psoriasis. Cultures were negative for patho-

gens. Biopsy showed structures characteristic of psoriasis. Therefore, a diagnosis of psoriasis was made. This diagnosis was based not on clinical and microscopic observations alone but on my former experience of seeing many patients with cement dermatitis while I was consulting surgeon for a large cement plant and, also, on the history that this man's condition showed no great improvement although he had not been working with cement for two years.

**A Case for Diagnosis** Presented by MAJOR Z. N. KORTH, M. C., A. U. S.

J. G., a white man aged 38, was admitted to the hospital Oct. 18, 1943, with an ulcerated lesion on the lateral aspect of the distal third of the right leg. His history revealed that while training a dog at the War Dog Reception and Training Center he sustained a rope burn in this area when the dog bolted and tried to get free. The skin was denuded and had a clean red area which oozed clear fluid. The area failed to heal, and he was admitted to a station hospital, where treatment was carried on until he was transferred to Walter Reed General Hospital. There had been no improvement, in fact, the lesion had become slightly worse.

On admission, examination revealed a rectangular lesion about 10 by 5 cm., which was elevated and sharply outlined. Throughout the lesion there were rather minute ulcerations, and the lesion was slightly boggy on palpation. Biopsy performed on Oct. 27, 1943 led to the diagnosis of chronic dermatitis with ulceration and one performed on November 19, to the diagnosis of chronic ulcer of the skin. Examination on these occasions failed to reveal any etiologic agents. Cultures were all negative except for staphylococci and streptococci. Wet dressings of solution of aluminum acetate were used, and the lesion finally healed. The patient was about to be returned to duty when there was a sudden recurrence, with extension to the surrounding tissue and development of many pea-sized ulcerations. Much edema developed, and the area became vividly erythematous. Aluminum acetate soaks failed to bring about improvement, and 10 per cent potassium iodide solution was used with almost immediate results. Thirty drops of potassium iodide three times a day by mouth brought about salivation and headache and had to be discontinued. At present the potassium iodide soaks are still being used. Roentgen ray therapy was not given at Walter Reed General Hospital, since the patient had had a total of 500 r prior to admission, without any change in the lesion.

Laboratory observations were not significant.

MAJOR Z. N. KORTH, M. C., A. U. S. Whatever the origin of the disease, the patient is a dog trainer in the Army. He has had fixed dressings for a period of two months absolutely fixed, so that he could not release them. The problem of malingering has been seriously considered because the eruption has recurred without any particular reason and for the past two months he has had fixed dressings.

CAPT. RICHARD L. SUTTON JR., M. C., A. U. S. This patient interests me greatly. I see numerous instances of this sort with soldiers, in whom dermatitis begins with chigger bites on maneuvers or a comparable trivial injury and develops into circumscribed spreading patches of a solid eruption, which does not manifest a tendency to heal in the center but slowly spreads by expanding and, apparently, also by autoinoculation. It itches severely, is exudative at first but tends eventually to become dry and lichenified and induces local hyper-

pigmentation. Then it does not change in months, except to become worse under treatment with some medicaments. Sulfonamide ointments applied during the early exudative stage, when the disease resembles ordinary infectious eczematoid dermatitis, induce sensitivity. I have seen patients in whom, months after the start of the disease, the administration of 0.5 Gm of sulfathiazole by mouth would cause bullous exacerbation of the lesions. Cultures of material in these bullae prove to be sterile.

I have followed 1 such case in particular for several months, using every facility at my command, liquid and unguent antiseptics, benzine, mercury bichloride baths, gentian violet medicinal, triple dye, iodine preparations, merthiolate, an ointment of benzoic and salicylic acid, 30 per cent sulfur ointment, salicylic acid and sulfur ointment and protective dressings. I have also avoided medication for adequate periods, in order to assess the value of doing nothing, which is often good dermatologic therapy. Scrapings from the lesions showed no parasites except hemolytic *Staphylococcus aureus*, although *Trichophyton purpureum* was diligently sought. Excised bits smeared over Petri dishes yielded only staphylococci. Yet penicillin in adequate dosage likewise failed to help. Roentgen ray therapy did help, though not in the conservative doses of 75 r to which dermatologists are accustomed, but in doses of 200 r. After about four such doses at seven day intervals, a lesion would disappear permanently. I am confident that adequate roentgen therapy will cure this patient even though approximately 500 r in small doses has been given. I wish that I knew the cause of this lesion, from which we have obtained only *Staph. aureus*, perhaps it is a lichenifying type of infectious eczematoid dermatitis. *Staphylococcus toxicod* will help patients with dermatitis infectiosa eczematoides, but it and autogenous vaccines have not helped my patients with "Dermatitis, lichenoid, chronic, disseminated, severe, cause undetermined."

DR MURRAY M. ROBINSON, Washington, D. C. During several years of practice in the service, I have seen many similar ulcerative lesions in soldiers. The history is fairly typical. The lesion frequently appears as a result of trauma due to pressure, such as is produced by government issue shoes. The soldier is admitted to the hospital, and after the use of fairly simple procedures, such as application of wet dressings, the lesion heals and the patient is sent back to duty. The trauma is duplicated, and the lesion returns. The patient is then readmitted to the hospital. This time the lesion is slow in healing and frequently fails to respond even to roentgen therapy. In some cases, satisfactory results were obtained from the use of 5 per cent scarlet red in paste of zinc oxide NF.

MAJOR Z. N. KORTH, M. C., A. U. S. This patient has had dressings since he was transferred to my ward about two weeks ago. Up until that time he was in my ward for only two nights. At the time that I saw him, about the middle of October, the lesion was slightly longer than now and definitely rectangular. The lesion occurred when the hound which the man was training pulled him and scratched the rope against his leg. At that time he failed to improve with the use of all types of therapy. Solution of aluminum acetate was applied, and a dressing was placed over it. The dressing could be identified by some marks placed on it. The patient was urged to return to change the dressing, and the eruption again broke out. He was sent to me about two weeks ago. He was given potassium iodide with a dressing which I am pretty certain he is not

getting changed. He has done fairly well under treatment with potassium iodide. He has been given some by mouth, but it had to be discontinued because of the symptoms arising. So far as roentgen rays are concerned, this man had three treatments prior to his admission to Walter Reed General Hospital, and he was referred to the radiologic department for further roentgenologic therapy, but the radiologist refused to go ahead with further treatment.

DR EUGENE F. TRAUB, New York. It is well known that the histories taken by different men can bring out entirely different points in the patient's story. I am sure that this fact will be appreciated when I say that on talking to this patient I gained an entirely different impression from that stated on his chart. If his story is reliable, he certainly has had nothing remotely resembling a sealed dressing since around last Thanksgiving or early in December. He stated that the lesion had almost entirely healed, and he was more or less left to his own devices. From about Thanksgiving until the present time he has applied his own medication with no medical supervision. The dressings were not sealed ones and were not applied in such a manner that malingering could be excluded. In fact, he stated that he put on the dressings himself. Therefore, while this may not at all be a matter of malingering, nevertheless I think that the exacerbations might well have been caused by scratching or by a dressing he has applied himself, sticking to the lesions in such a manner that when it is pulled off it causes more irritation than it does good. For this reason I believe that the eruption can largely be explained on an artificial basis.

DR MAURICE J. COSTELLO, New York. I believe that this patient may have an ulcerative undermining infection of his skin caused by the microaerophilic hemolytic streptococcus. Proper bacteriologic studies for anaerobic organisms should be performed. I suggest that fresh zinc peroxide medicinal in an ointment base be applied and that it be covered with wet gauze and sealed with a petrolatum gauze dressing.

DR FRED WEIDMAN, Philadelphia. I do not believe that this is a factitious lesion, because there are some pustules around its edge. It would be hard for the patient to induce these himself. In view of the indolent type of reaction, I am reminded of the characteristics of a microaerophilic streptococcus infection, such as Meleney has written about, for which zinc peroxide medicinal is indicated therapeutically.

DR BERNARD APPEL, Lynn, Mass. I suggest a real old time dressing which I have used many times successfully, the so-called hourglass bandage. It consists of putting on whatever dressing is appropriate, lightly medicated. Several layers of cellulose tissue paper are placed on top of this, so as to encircle the entire limb at the site. Then ordinary loose mesh cotton bandage is applied in moderate thickness and extent, usually not less than six or eight layers. Then several coats of water glass are painted on in succession, from four to six applications are usually sufficient. This water glass is the household solution of sodium silicate in which eggs are usually preserved. The resultant cast is light and strong and comfortable, tamper proof and easily removed. This bandage could be used if it turns out that the patient has dermatitis factitia and it becomes advisable to use an occlusive dressing.

CAPT RICHARD L. SUTTON JR., M. C., A. U. S. I apologize for speaking twice during the discussion of 1 case. I have managed more than a dozen cases like this in Army hospitals. Wet dressings with hydrogen

peroxide or sodium perborate did not help Plaster casts have not helped Adequate roentgenologic therapy does help

MAJOR Z N KORTH, M C, A U S I wish to corroborate what Captain Sutton says This man has had zinc peroxide medicinal He has had sodium perborate It is possible that I may convince the authorities at the hospital to give him more roentgen therapy At least, I will do my utmost

**Amyloidosis Cutis** Presented by DR HERMAN KITTREDGE, Washington, D C

C P K, a white man aged 74, (mentally defective) is said to have had lead poisoning when young but to have made a good recovery Considerable portions of both legs are studded with mostly discrete, brownish yellow, hemispherical, interfollicular papules which are 2 to 5 mm in diameter, dry, hard and glassy. Some are scaly at the summits

Injections of 1 per cent solution of congo red, administered both intracutaneously and subcutaneously four years ago gave positive results Subcutaneous injection of 1 cc of the same dye in the posterolateral aspect of the right calf was given subcutaneously yesterday with the result seen today After intravenous injection of congo red a week ago as a test for systemic amyloidosis, the serum lost 33.4 per cent of the dye after one hour, which, according to Levinson and McFate, is inconclusive

Laboratory determinations were within normal ranges Biopsy has not been performed recently, but sections prepared and studied four years ago by Dr Ruben Nomland, of the University of Iowa, all showed deposits of amyloid, the stains used being methyl violet, Giemsa, Van Gieson and hematoxylin and eosin The amyloid stains have, of course, faded in the three accompanying sections, which now show only the general histologic structure

The patient had four or five fractional doses of unfiltered roentgen rays four years ago, when the itching was severe, but he has had no subsequent treatment This therapy relieved the itching

#### DISCUSSION

CAPT RICHARD L SUTTON JR, M C, A U S Lichen amyloidosis is an extremely pruritic disease In addition to the amyloidosis demonstrated by reliable tests, I believe that the patient manifests a lack of vitamin A

**Granuloma Inguinale** Presented by DR FRANK J EICHENLAUB, Washington, D C

D K K, a Negro man 37 years old, first noted in October 1938 a small nodule on the left side of the anterior perineum It gradually enlarged, and at times small nodules would appear and coalesce with the original growth In February 1939 the patient went to the Health Department Clinic for treatment A serologic reaction of 3 plus was obtained, and injections of arsphenamine and a bismuth compound were given until April 1940 During this time a lesion developed in the right perianal region, and all the lesions had remissions and exacerbations The lesions were oval in outline above the surface of the skin and had the color of red meat

The patient was admitted to Gallinger Municipal Hospital in May 1940, and intramuscular injections of Fuadin were given for five weeks All the lesions healed and the patient was discharged to the clinic In April 1941 two new lesions developed in the vicinity

of the old ones Since the patient was unable to secure treatment for about a year, the new lesions coalesced with the older ones On readmission to Gallinger Municipal Hospital in July 1942, all the involved areas again had the appearance of red meat The patient was given injections of a bismuth compound and Fuadin for eight weeks with no apparent improvement, and he was again discharged to the clinic

He returned to the hospital again in June 1943, because of a gradual spread of the lesions He was given 20 per cent podophyllum in olive oil topically and freshly prepared 2 per cent solution of antimony and potassium tartrate, intravenously, twice weekly for eight weeks Decided improvement was noted, and the patient was again discharged to the clinic for injections of Fuadin He was again hospitalized in December 1943, as the lesions were larger He has been receiving podophyllum and Fuadin

There is a linear lesion 4 by  $\frac{1}{2}$  inch (10.2 by 1.3 cm) on the left anterior side of the perineum, studded with areas of depigmentation and redness On the right side of the perianal region there is a plaque 3 by 2 inches (7.6 by 5.1 cm) of red, healing granulation tissue, the lateral border of which is scabbed

The laboratory determinations were as follows the Frei and Ducrey tests elicited negative results on two different occasions, the Kahn reaction in 1939 was 3 plus, in 1943 it was negative The urine was normal In June 1943 the red blood cell count was 4,160,000, the white blood cell count was 5,500, and the hemoglobin content was 80 per cent In January 1944 the white blood cell count was 6,550, and the hemoglobin content was 98 per cent

On biopsy, leishmania bodies were found

**Mycosis Fungoides** Presented by DR FRANK J EICHENLAUB, Washington, D C

C M, a Negro man 31 years old, has a lesion which started on March 17, 1942 as two white pea-sized nodules in the upper part of the intergluteal fold After about two months, the lesion broke down and began to spread until the entire fold was involved, which took about three months The patient went to Providence Hospital, where the entire area was excised About this time he noticed a kernel in the right groin The excised area around the anus healed and broke down again in four months Then for about a year he went to a private physician, who gave him Fuadin intramuscularly and neoarsphenamine intravenously There was no response to this treatment All during this time the right inguinal lymph node gradually enlarged and started to drain

The patient came to Gallinger Municipal Hospital Jan 5, 1943, because the lesion around the anus was draining profusely and because a nodule was developing in the right inguinal region During the hospital stay the nodule broke down completely, and soon the patient noted "red meat" being formed After one month of hospitalization, the left inguinal node enlarged and broke down and healed in about three months The patient was in Gallinger Municipal Hospital until August 1943 He was given podophyllum topically and antimony and potassium tartrate (2 per cent freshly prepared solution) intravenously twice a week and a few injections of Fuadin All granulation tissue had disappeared

After discharge this man went to Providence for clinical treatment and there received Fuadin Around Christmas 1943 a nodule again appeared in the right



groom, which soon broke down, and new granulation tissue began forming around the anus

In the right groin there is a granulating ulcer, 2½ by 1 inch (6.5 by 2.5 cm), consisting of bright red tissue and a serosanguinopurulent discharge. Around the anal region there is a reddened, granulating ulcer 5 by 3 inches (12.7 by 7.5 cm) and some smaller ulcers extending down onto the posterior surface of the scrotum

Laboratory determinations in 1943 included negative reactions to the Frei and the Ducrey tests and a negative Kahn reaction six times from 1941 to 1944. In 1944, the Frei and the Ducrey tests elicited negative reactions on two occasions

Biopsy showed the presence of leishmania bodies

#### DISCUSSION OF THE TWO PRECEDING CASES

DR D C A BUTTS, Washington, D C. What I have to say is merely an expression of ideas which have apparently been borne out by certain observations which I have repeatedly made, not only in the 10 cases tabulated here but also in a series of 8 cases studied in 1937 and in advanced cases which I recently had occasion to see in Trinidad and British Guiana. However, the statistics which I shall present are based entirely on the 10 cases studied here in Washington, 2 of which you had an opportunity to observe this morning

Seven of the patients showed the presence of leishmania bodies. Six of the 7 patients gave a history of having had a Phthirus pubis (crab louse) infestation from a minimum of one month to a maximum of eight months prior to the onset of their disease. The only exception to this observation was a woman patient. Thus more than 85 per cent of the patients showing leishmania bodies had had crab lice eight months or less before the onset of the gross lesion. The 3 patients in whom leishmania bodies could not be found gave a history that was negative for louse infestation. In 2 of the 7 patients (28.6 per cent) the external genitalia were initially involved, and in the remaining 71.4 per cent the initial changes appeared in the inguinal or perianal regions, which are the ones most frequented by the crab louse

Of the 7 patients showing the presence of leishmania bodies, 4 (or 57 per cent) also showed during dark field examination the presence of an active spiral and also a motile coccobacillary form of organism. Unfortunately, dark field studies were not possible for all 7 patients. The 3 patients who did not show the presence of leishmania bodies were likewise lacking in the spiral and motile coccobacillary forms. These observations were previously reported by me in 1937 (Butts, D C A. Granuloma Inguinale, Preliminary Report on Certain Microscopic Observations *Am J Syph, Gonorr & Ven Dis* 21:544 [Sept] 1937). In 1939 Dr Robinson, in discussing Dr Greenblatt's paper (Greenblatt, R B, Dienst, R B, Pund, E R, and Torpin, R. Experimental and Clinical Granuloma Inguinale *J A M A* 113:1109 [Sept 16] 1939), made a statement that the spiral forms reported by me were of the perfringens type and that the motile bacteria were fusiform bacilli. Dr Robinson went on to say that if the material was obtained from the base of the lesion only leishmania bodies would be found. I might add that if one is to assume that the spiral and bacillary forms are contaminants, then one must also make the same assumption concerning the leishmania bodies, because they are generally found together in the same smears. I regret that I did not clearly state in my preliminary report in 1937 that the material had always been removed from the base of the lesion

Always spiral and motile rod forms were found, whether or not leishmania bodies were observed. The exact nature of the leishmania body is still questionable. It seems possible that it may be a sporozoon, similar in some respects to the coccidium or to the plasmodium, or it is not beyond the stretch of the imagination to theorize that the spiral form and the rod form reported by me and the intracellular organisms (leishmania bodies) are transformations of the same organism. It is my hope soon to conduct some louse transmission experiments and, at the same time, to make intensive bacteriologic studies on the lice removed from infested patients. Also I hope to continue my studies on the nature and significance of the organisms observed in lesions of granuloma inguinale

• DR REUBEN GOODMAN, Washington, D C. The only flaw in the theory is that pediculosis pubis in Negroes is actually unheard of. I have yet to find a case of it myself

DR H H HAZEN, Washington, D C. At Freedmen's Hospital we have had the opportunity to study over 75 patients with granuloma inguinale. All but 3 of them had positive serologic reactions for syphilis, and the vast majority of these results were confirmed in another laboratory. It would seem that granuloma inguinale should be included among the ever growing list of diseases that cause a positive serologic reaction. The second point is the one in which Dr Goodman has forestalled me. During thirty-five years of work at Freedmen's Hospital, only five times has a case of pediculosis pubis been encountered in either the clinic or the wards, and pediculosis corporis is equally rare, despite the fact that the diseases have been carefully looked for

DR D C A BUTTS, Washington, D C. One more word about the incidence of Phthirus pubis infestation among Negroes. My figures certainly do not coincide with those of the other two speakers. I do find it difficult to get Negroes to give an honest history. However, if they do, many of them will give a history of louse infestation

#### LOS ANGELES DERMATOLOGICAL SOCIETY

WILLIAM H GOECKERMAN, M D, *Chairman*

CLEMENT E COUNTER, M D, *Secretary*

March 14, 1944

#### Lupus Erythematosus, Discoid Type Presented by DR CLEMENT E COUNTER

M C, a woman aged 46, began to have the present inflammatory eruption of the face about seven years ago. The first lesion appeared on the lower part of the face and was approximately the size of a dime. Since then it has enlarged to its present size and new similar lesions have occurred on the sides of the face just below the ears. About 1918 the patient had syphilis and received approximately six months' therapy, which included injections of mercurials and potassium iodide by mouth as well as six to eight intravenous injections of arsphenamine. The Wassermann reaction became negative and has been negative ever since

There are defined erythematous patches on the lower part of the face, including chiefly the chin and the upper lip, entirely surrounding the mouth. Other similar lesions are present on the sides of the face just below

the ears. The lesions are red and papular and have fine clinging scales. In places, there are dilated pores. The central portion of the lesions tends to be brownish and to exhibit considerable atrophy.

Examination of the chest eighteen months ago failed to reveal any evidence of active tuberculosis.

The Wassermann reaction of the blood was negative, and results of an examination of the spinal fluid two years ago were entirely negative.

A biopsy performed in February 1942 of one of the lesions below the left ear revealed perivascular infiltration in the upper part of the corium. There were hyperkeratosis and plugging of the follicles, together with acanthosis in the epidermis, all of which are consistent with lupus erythematosus.

Gold sodium thiosulfate and bismuth subsalicylate have been given in groups of from twelve to sixteen weekly injections. The injections of gold began with 5 mg and increased so that later injections of a given group have been 50 mg doses, and the bismuth has been given in 0.13 Gm doses.

For the past four months she has been using a diet in which sodium chloride has been almost entirely eliminated. In addition, she has taken 9 grains (0.58 Gm) of quinine sulfate by mouth daily for eight weeks at a time on two occasions.

This case is presented for therapeutic suggestions.

#### DISCUSSION

DR H C L LINDSAY I suggest giving the patient neoarsphenamine. I presented 2 patients with lupus erythematosus both of whom had clearing with neoarsphenamine. Both of these patients had had indifferent results from therapy with bismuth and gold salts which had been given for over a dozen years.

DR SAMUEL AYRES The patient said that she had some kind of pelvic trouble a number of years ago, and she complains of some discomfort. I wonder whether a focus of infection might be present in the pelvic area.

DR CHRIS HALLORAN Regarding the treatment of lupus erythematosus with neoarsphenamine, many of you may remember a patient at the Los Angeles County Hospital whose disease was recalcitrant to treatment and to whom I gave neoarsphenamine. After the first few injections the eruption became disseminated. The patient later had considerable improvement with injections of liver extract intramuscularly.

DR W H GOECKERMAN Years ago while I was at Mayo Clinic I treated several dozen patients with neoarsphenamine, and I found it of no use. I discarded it at that time because I had an experience similar to that of Dr Halloran.

DR KENDALL FROST If one will consult Schamberg's original paper on therapy with gold, he can learn something on dosage. I think that sometimes we do not use gold to its fullest therapeutic potentialities. Schamberg, I believe, advocated 100 mg twice weekly as the maximum dose.

DR M E OBERMAYER I am glad that Dr Frost brought up the question of dosage. There has been a tendency for us to be overcautious because of the possibility of serious toxic reactions, particularly from gold sodium thiosulfate. Such reactions can be minimized by preparing the patient for gold therapy by means of a course of injections of liver extract. I prefer the use of a gold compound of low toxicity, such as the ammonium salt of succinimidoauric acid, a compound which was prepared by Kharsh and Isbell, of the Department of Chemistry of the University of Chicago, and studied by S W Becker and me (Obermayer,

M E, and Becker, S W. Ammonium Succinimido-Aurate, a Gold Compound of Low Toxicity, *J Invest Dermat* 1 85, 1938). When used for lupus erythematosus, this compound shows a therapeutic effect similar to, but perhaps slower than, that of gold sodium thiosulfate, but untoward reactions are much less frequent and certainly less serious than those from other gold compounds. It has a gold content of 28.4 per cent. Individual doses range from 200 to 400 mg, but even considerably higher doses can be given without toxic manifestations. Because the drug is more rapidly excreted than is sodium thiosulfate, it may be advisable to administer it twice instead of once weekly. Ammonium succinimidoaurate can be obtained on application to Dr Ben Sher, 912 Margate Terrace, Chicago.

#### A Case for Diagnosis (Lichen Planus with Atrophic Lesions, Lichen Sclerosus et Atrophicus of Hallopeau?) Presented by DR HAL E FREEMAN

W C W, a man aged 58 has an eruption which began about seven years ago and has been persistent ever since. It is asymptomatic.

The present examination reveals more than twenty-five flat, only slightly raised, firm white papules on the flexor surface of the left wrist.

The patient has taken thyroid extract for about three years.

The Kahn test of the blood elicited a negative reaction. The study of the blood cells revealed nothing significant, and the urinalysis gave negative results.

#### DISCUSSION

DR NELSON PAUL ANDERSON I object to the diagnosis of lichen planus. This is a classic case of Hallopeau's lichen sclerosus et atrophicus. I think that one gets onto debatable ground when the diagnosis of lichen planus also is made.

DR SAMUEL AYRES JR The lesions on the left wrist showed only atrophic types. There were lichenoid lesions which showed definite atrophy, but on the left wrist I saw two lesions definitely characteristic of lichen planus. They were shiny papules of a violaceous color.

DR STANLEY CHAMBERS' I should like to support Dr Ayres' conclusions.

DR PAUL FOSTER This man stated that he had had somewhat similar lesions on the penis several times in the past. That, in conjunction with the lichenoid appearance of the present lesions on his wrist, would suggest the possibility of lichen planus. The distribution of the primary lesions is unusual, being of a cartwheel type. This suggests dermatitis factitia.

DR HAL FREEMAN From the literature I found that lichen sclerosus et atrophicus produces papular lesions with a central hyperkeratotic plugging. Some authors consider lichen planus with atrophic lesions and lichen sclerosus et atrophicus synonymous. I thought that some one might mention a scleroderma guttatum.

#### A Case for Diagnosis (Xanthelasma Papulosum Multiplex?) Presented by DR MAX POPPER (by invitation)

H L is a woman whose past history reveals that as a child she had scarlet fever and pneumonia. More recently she has had cholecystitis, arthritis and heart trouble. There have been two rectal operations in the past two years. Abscessed upper teeth were removed three years ago. There was an appendectomy thirty-



five years ago Five years ago there was a uterine curettement for the treatment of a chronic discharge A miscarriage occurred seventeen years ago She has had syphilis She completed two years of antisyphilitic treatment about seven years ago The Wassermann reaction of the blood was strongly positive eight years ago, but it has been negative since then The Wassermann reaction of the spinal fluid was negative

The present lesions made their appearance on the right buttock two weeks after the healing of what seemed to be the fourth attack of herpes simplex on the same area This was six months ago There was no sensation of itching or tenderness early in the course of the disease, but more recently there has been tenderness enough to produce pain on sitting

The lesions are undergoing spontaneous improvement As regression takes place, papules become bluish, less elevated and eventually ill defined dull red macules

The chief lesions are located on the buttocks and backs of the thighs Some lesions extend around the thighs and downward to the vicinity of the patella There are more lesions on the right than on the left There are scattered lesions on the right arm and forearm and on the palms and wrists and a few on the legs, but the face, trunk and left arm are free Individual lesions are 2 to 5 mm in diameter and raised about 2 mm above the general surface of the skin The lesions are firm and red and do not tend to be confluent even where they are most numerous

Quantitative determinations of the blood cholesterol have been normal Quantitative determinations of the blood sugar have all been normal, including determinations when the patient was fasting and when given a measured amount of sugar in the sugar tolerance test The urine has also been normal

A biopsy revealed in the corium increased amounts of fibrous tissue infiltrated with xanthoma cells and a few lymphocytes

#### DISCUSSION

DR NELSON PAUL ANDERSON The microscopic section is typical of xanthoma

DR HAL FREEMAN I should certainly like to hear some discussion on the infectious nature of the disease I am not acquainted with an infectious element in xanthoma

DR SAMUEL AYRES I had the opportunity of seeing this patient with Dr Popper a month or two ago At that time the lesions looked like the usual ones of xanthoma diabeticorum Apparently a competent internist said there was no diabetes, although the dextrose tolerance test at the end of four hours showed 138 mg of sugar per hundred cubic centimeters of blood This would suggest some kind of a metabolic irregularity, even though one might not call it true diabetes The lesions are small, suggesting this type of disease Whether it is to be segregated from the true xanthoma diabeticorum I am not sufficiently acquainted with the problem to say

DR MAX POPPER (by invitation) I want to point out that the start of the disease was peculiar About five months ago the patient had an inflammatory process on the right buttock, a redness with swelling and pustules Three weeks later this rash disappeared, and two weeks later a papular eruption developed, starting on the same site and gradually spreading on both buttocks and going down the thighs Then I examined the histologic picture It showed circumscribed nodules infiltrated with foam cells Now you have seen a comparative picture Most of the papules have almost disappeared They are flat and the yellow color is almost

gone I could not find a case of similar type in the literature No treatment was given I consider that the disease is a self limited inflammatory process in which the infecting agent, supposedly a virus, causes a change in the invaded cells so that the cells can store lipid substances temporarily The localization was chiefly on the buttocks and thighs, with a few lesions on the elbow and right arm

#### A Case for Diagnosis (Progressive Pigmentary Dermatositis [Schamberg's Disease]?) Presented by DR HAL E FREEMAN

D M, a man aged 22 years, began to have an eruption on the anterior surface of the right leg about five years ago This has progressed since then It is asymptomatic There is no history of injury initiating its onset

There is an erythematous squamous eruption approximately palm sized on the anterior surface of the right leg This is reddish brown and shows telangiectases It is macular and papular, and its margins fade into the normal surrounding skin

The time of bleeding and clotting of the blood were normal The hemoglobin content of the blood was normal A blood count revealed normal numbers of red and white cells On examination the urine was normal Kahn and Hinton reactions of the blood were negative A determination of ascorbic acid in the blood revealed 1 mg per hundred cubic centimeters

#### DISCUSSION

DR CHRIS HALLORAN If this is a case of the so-called progressive pigmentary dermatosis of Schamberg, it does not conform clinically to the ones I have seen This patient presents a palm-sized lesion on the shin, and there is another lesion, of the size of a coin, on the ankle In the cases of Schamberg's progressive pigmentary dermatitis which I have observed the eruption began about the ankles and sprayed upward over the lower third of the leg

DR M E OBERMAYER Purely clinical discussions of such cases without microscopic sections are futile I suggest a biopsy

DR NELSON PAUL ANDERSON Whenever a case of Schamberg's progressive pigmentary dermatosis is presented, I am reminded of the remarks of Dr Henry Michelson, who said that he knew of no other eruption more productive of futile discussion than this In this particular patient, who is rather young to have a stasis dermatitis, these lesions are actually due to trauma This man works at a job where his right leg every now and then gets a blow from a metal bar I believe that this trauma is the cause of the cutaneous changes over the shin I suspect that the lesion on the ankle is probably due to some other type of injury I have not the slightest idea what has caused the lesion on the left leg I think that most of the pictures of capillaritis which one sees on the legs are either a stasis dermatitis or due to some trauma As regards therapy, I should like to suggest the administration of ascorbic acid I have observed considerable benefit from this vitamin in some recent cases in which the capillaritis was bilateral and widespread, extending from the ankles to the knees

#### A Case for Diagnosis (Synovial Pseudocysts?) Presented by DR M E OBERMAYER

B K, a young private in the Army, has had tender nodes on the right heel, the plantar surface of the great toe and the anterior portion of the right sole for five

months. The pain has varied. On some days it was pronounced, on others, absent. He thought that he noticed an increase in the size of the lesions. After my examination he was transferred to Bushnell General Hospital, Brigham City, Utah, to the care of Captain W J Marginson. Additional subcutaneous nodes were found present on the patient's buttocks. Nodes were removed for biopsy from the right hypothenar region and from the right gluteal region.

The examination shows tender subcutaneous nodules which vary from 1 to 3 cm in diameter on the sole and the plantar surface of the right great toe and over the articulations between the distal and the adjacent phalanges of the index fingers and thumbs as well as in the hypothenar region. On palpation these lesions seem to be fluctuant.

A tentative diagnosis of synovial pseudocysts was made, but treatment was not applied.

The section from the lesion in the gluteal region showed a slight local fibrosis and a small amount of a cellular infiltrate consisting of a few lymphocytes, mononuclear cells and an occasional plasma cell loosely arranged in a small cluster. The section from the hypothenar region showed no abnormal changes except a few lymphocytes close to the epidermal-dermal junction. The comment by the chief of laboratory service, Lieut Col F B Queen, was "The cause of neither of these lesions is clear. The lesion from the gluteal region might be healed suppurative panniculitis. This is purely speculation, as it cannot be so diagnosed from the lesion itself. The nature of the hypothenar lesion is unknown." The sections were reviewed by the Army Medical Museum, in Washington, D C. The comments by Lieut Col Baldwin Lucke are "The lesion from the hand is suggestive histopathologically of keratoderma palmare. The genesis of the fibrosis in the subcutaneous fat of the biopsy from the gluteal region is not clear to us either. There is a concomitant nonspecific low grade dermatitis."

The slides presented were loaned to me by courtesy of Captain W J Marginson, M C, A U S.

#### DISCUSSION

DR HAL FREEMAN I propose the diagnosis of dermatomyositis.

DR SAMUEL AYRES I have no clear concept of the lesions. The closest would be some type of inflammatory process. Apparently none of these lesions have progressed or regressed. None of them have become very large. The largest one is on the buttock. The lesions are rather vague and rather deep.

DR M E OBERMAYER When this patient was first seen, he did not tell me about the nodules on his hips, and, as the lesions on his fingers gave the impression of being slightly fluctuant, I thought of the possibility of synovial pseudocysts. With this preliminary diagnosis he went to the Army hospital where his eruption was extensively studied. Unfortunately, the microscopic picture of the excised lesions is as little characteristic as the clinical appearance. I agree with Dr Ayres that the process is undoubtedly one which involves the subcutaneous tissue, but there is not sufficient evidence to call it nonsuppurative panniculitis, though the disease may belong to this rather ill defined group of dermatoses.

#### Lupus Erythematosus and Psoriasis Coexisting in the Same Patient Presented by DR KENDAL FROST

E E a woman aged 57 has had lesions on the right cheek since the summer of 1942. Similar lesions have

come and gone on the nose and left ear for two years. She has had hard red scaling lesions on the right elbow for more than ten years.

Around the eyes and across the nose are several erythematous sharply margined scaly lesions. There is slight atrophy and telangiectasia. On the right elbow is an infiltrated erythematous scaly papular plaque typical of psoriasis. There are pitting and irregular deformity of the nails.

Biopsy of a facial lesion showed a moderate amount of perivascular infiltration and a tendency to disorganization of the basal cell layer. Large follicular plugs were present in the hyperkeratotic epidermis.

Improvement in the facial lesions was produced after she was given injections of gold and bismuth preparations from February to August 1943. She took a rest from treatment on her own advice. In November 1943 there was a relapse. She was then given bismuth and liver intramuscularly at weekly intervals for ten weeks, with no improvement. Medication was changed to gold in February 1944. The lupus erythematosus lesions on the face have improved considerably since then.

#### DISCUSSION

DR CHRIS HALLORAN I agree with the diagnosis. The lesions of the elbow are certainly psoriasis, and that of the cheek clinically is lupus erythematosus. A few years ago I saw a patient with a small plaque on the bridge of the nose, the center of which looked epitheliomatous. A biopsy showed epithelioma. The entire small plaque was destroyed. Recently the patient has returned with typical lesions of lupus erythematosus on both sides of the bridge of the nose.

DR M E OBERMAYER I had the opportunity of seeing this patient several times before the biopsy was performed, and I did not believe then that she had lupus erythematosus but considered her facial lesions part of her psoriasis. Examination of the microscopic section, however, has convinced me that Dr Frost's original diagnosis was correct.

DR L F X WILHELM I wonder whether the patient had psoriasis before the lupus erythematosus and, if she did, whether the use of sun treatment could have been a large factor in the onset of the lupus erythematosus.

DR NELSON PAUL ANDERSON It is difficult to make a diagnosis of two cutaneous diseases at one time when both are of an inflammatory nature. I believe that the lesions on the face are the same as those on the elbows. I looked at the section but did not study it carefully. However, I did not feel that it was typical of lupus erythematosus. Whether the patient has psoriasis or not I am not prepared to say. There are psoriasiform lesions on the elbow, but whether they are true psoriasis or not I do not know.

DR PAUL FOSTER Some years ago, Dr McKee and I wrote a paper called "The Aberrant Lesions of Psoriasis." We found that in psoriatic patients there were many lesions which did not take the form of psoriasis but frequently took the form of lichen planus or lupus erythematosus. We made biopsies of all these lesions, and it was our experience that the study of the microscopic slide confirmed the diagnosis from the clinical appearance of the lesion. It seems to me that about 4 per cent of the patients had lesions which appeared to be lichen planus and about 2 per cent had lesions which appeared to be lupus erythematosus. Drs Frazier and Satenstein confirmed our study of those microscopic sections.

DR W H GOECKERMAN Several years ago Dr Montgomery and I presented such a case before a number of dermatologic societies. The discussions always varied. We had several biopsies, and Dr Montgomery was never satisfied with a diagnosis. I published the report anyhow, because it was an unusual case (Goeckerman, W H. Psoriasis Associated with Lupus Erythematosus, *M Clin North America* 15: 1491-1496 [May] 1932). Some who saw the patient favored the diagnosis of lupus erythematosus, others were inclined to the diagnosis of a combination of lupus erythematosus and psoriasis to explain the eruption.

DR KENDAL FROST I feel that these processes are separate. The patient has had the psoriasis on the elbows and the changes of the nails for many years and the facial lesions only two years. I should have a biopsy specimen from the elbow as well as from the face, and the study of the two would clarify the situation. The lesions of the elbow and finger nails have cleared considerably in the last few weeks after some roentgen ray treatments. I do not see why a person cannot have two chronic inflammatory skin diseases at the same time. Her facial lesions were almost clear last fall, when she voluntarily stopped treatment. She later returned with the process showing considerable activity. She did not respond to bismuth but has responded to gold. I do not think the lupus erythematosus and the psoriasis lesions are related.

#### Herpes Simplex of Buttocks Presented by DR PAUL D FOSTER

B B, a white woman aged 58, presents several reddish macules on the right buttock. Some of these appear to be of recent origin, while others are older and faded. Otherwise her appearance is that of a healthy woman. A general examination failed to demonstrate any abnormality.

About five years ago a group of stinging, burning lesions  $\frac{1}{2}$  inch (1.3 cm) in diameter first developed on the patient's right buttock. Those lesions stayed for a week and disappeared. Six months later she had similar lesions on the buttocks. Since then there have been many recurrences. These have been especially numerous in the past two years. Two years ago she was given some injections of a bismuth preparation, which seemed to help. Then she was given smallpox vaccine and fractional doses of roentgen radiation weekly for six weeks. Then there were no lesions for one year, but they have recurred again in the past six months. She had herpes zoster two years ago.

A blood count, urinalysis and determination of blood sugar gave normal values. Kahn and Kline tests of the blood elicited negative reactions.

#### Herpes Simplex of Buttocks Presented by DR PAUL D FOSTER

W W S, a woman aged 50, has never been seriously ill. Three years ago she began to have "blisters" on each buttock which "swelled up, felt hot and itched." She applied various remedies, such as calamine lotion and proprietary medicines. The lesions would subside and she would feel well, but the site of healed lesions would remain red. She had many exacerbations from two to six weeks apart and noted that the lesions were becoming more and more extensive, with more and more intense itching.

The patient is a healthy-appearing woman. She is intelligent and cooperative. There are erythematous plaquelike lesions over the buttocks and right thigh and in the intergluteal fold. On the left side there is a group of vesicles on an erythematous base. Only moderate dental caries are noted in the general physical examination. The results of laboratory examinations are all normal, including determination of hemoglobin, erythrocyte count and leukocyte count, urinalysis and determination of blood sugar. The Wassermann and Kahn reactions of the blood were negative.

In the past three months she has received nine 75 r doses of roentgen therapy localized to the buttock lesions. Seven weekly vaccinations by the intradermal method were performed. She has shown decided symptomatic improvement, with progressive objective healing. Local applications were limited to the use of an antipruritic powder shake lotion. Decided improvement has been achieved.

#### DISCUSSION OF THE CASES OF HERPES SIMPLEX

DR H C L LINDSAY I agree with the diagnosis. I think it would be pretty hard to do anything of a therapeutic nature except with the vaccine.

DR M E OBERMAYER I have been interested for many years in the problem of recurrent herpes simplex. That the herpes virus is more prevalent than has been appreciated is shown by the high incidence of herpes simplex in patients receiving fever therapy. The absence of clinical lesions during the herpes-free intervals does not necessarily mean that the virus is not present in a latent stage. If it is assumed that it is living in the skin and becomes activated only under the influence of multiple precipitating factors, of which high temperature is one, it should be feasible to demonstrate its presence in loco during the latent stage. A method for doing this would be to mark one of the repeatedly involved sites with some indelible material, remove a biopsy specimen during the latent stage and inject tissue juice obtained from the specimen into a rabbit's cornea. The subsequent development of herpetic encephalitis in the rabbit would establish the presence of the virus beyond any doubt.

DR PAUL FOSTER These cases of persistent herpes simplex puzzle me. I have done everything I know of for the patients, and the lesions still remain. Neither of these women has been free of herpes at any time since I have seen them. One has been observed for three years and the other for five years. I have given one of them injections of smallpox vaccine beneath the areas on the buttock up to 0.5 cc per injection. They have been treated daily for four weeks at a time. Each of them has had a full course of roentgen therapy and autogenous transfusions, and I did not know what else to do. I will try Dr Obermayer's suggestion and report what happens.

#### A Case for Diagnosis (Mycosis Fungoides, Leukemia Cutis?) Presented by DR SAMUEL AIRES JR

I S, a woman aged 73, presents an eruption widely scattered over the trunk and to a less extent on the arms. It consists of some ill defined lesions and other sharply defined erythematous plaques. Their size ranges from that of a dime to that of a palm. Some are superficial, and some are infiltrated. The infiltrated lesions are scaly. There are several such lesions on the soles.

The amount of hemoglobin and the number of erythrocytes and leukocytes were normal. Direct microscopic examination of scales from the soles failed to reveal fungi. A biopsy bears out the clinical impression of lymphoblastoma. In the cutis there is a zone of round cell infiltration having the tendency of grouping into "nests."

The generalized itching eruption began about two years ago. There was a thyroidectomy twenty years ago. The present illness began with an oval lesion under the right arm which gradually enlarged. Then new lesions began to appear on the trunk. Some fractional doses of roentgen radiation have been applied. A powder shake lotion has been used locally, and use of phenolphthalein-containing medicaments has been discontinued.

## DISCUSSION

DR A FLETCHER HALL I thought that the plaques were suggestive of mycosis fungoides except for the color, and I assume that that has been changed by the roentgen ray treatment. It was otherwise clinically suggestive of that disease.

DR SAMUEL AYRES I should appreciate hearing whether any one has anything else to suggest except roentgen rays. Has any one used sulfonamide compounds for treatment of diseases in the lymphoblastoma group? (No one had used sulfonamide compounds.)

**A Case for Diagnosis (Seborrheic Dermatitis?)**

Presented by DR PAUL D FOSTER

J H B, a man aged 28, three years ago began to notice the development of the lesions on the sides of the nose which he now presents. In a few months these had spread over the face and forehead, and later they appeared on the back of the hands. He presented himself for treatment in April 1943, and he was completely cleared in August 1943. Four months later the lesions recurred on the back of the neck, and since then they have spread over the face, axillas, forehead, hands and forearms. Constant peeling and itching is characteristic of all lesions. Roentgen therapy has been used locally. The patient has received a preparation containing arsenic and bismuth given intramuscularly.

His general appearance is healthy, and he is intelligent and cooperative. He has numerous maculopapular erythematous patches which are slightly scaly. They range from 1 to 3 cm in diameter and are distributed over the face, forehead and arms. The general physical examination reveals normal conditions. Results of all laboratory tests, including erythrocyte and leukocyte counts, hemoglobin determination, urinalysis and blood sugar determination, were normal. The Wassermann and Kahn reactions of the blood were negative.

## DISCUSSION

DR MAX POPPER (by invitation) I have seen a rather large number of patients with eruptions which started out as a seborrheic dermatitis and then developed into lupus erythematosus. None of these had atrophy, and the eruptions seemed more closely to resemble dermatitis seborrheica, because the patient had an extensive seborrhea of the scalp at the same time. I should treat the scalp at the same time.

DR CHRIS HALLORAN In some respects the lesions suggested lupus erythematosus, but in others they strongly suggested seborrhea. One does not expect to see seborrhea in a circinate, plaquelike arrangement.

DR A FLETCHER HALL Although lupus erythematosus and seborrheic dermatitis come first to one's mind on observing this case, I was not satisfied with either diagnosis. The man works in a supervisory capacity on the production line in an aircraft factory. He has been given patch tests with zinc chromate in dry form, with a negative reaction. The resins in this primer cause capricious types of contact dermatitis, and, although this eruption is not typical of the type one usually sees from the resins, I think that he should be given patch tests with them, although he says that he had a negative reaction to the scrapings. When the resins do produce a dermatitis, a great many things suggest that it is produced by vaporized resins. The eruption appears particularly around the face, nose and eyelids, where this man has constant trouble. This eruption has disappeared at times and then reappeared. We have found that it acts in this way sometimes, depending on the freshness of the primer coat on the metal when it gets to his station. Such a dermatitis may be present for long periods when the metals are freshly coated, and then, owing to some change in the production schedule, the primer will be drier when it gets to him and the dermatitis will subside. People who do the drilling have this dermatitis constantly, but a foreman, such as this man, may not have such constant contact. It does come and go. I believe this is consistent with a dermatitis of that origin, and I would suggest that he be tested to the resins.

DR HAL FREEMAN On examining this patient, I thought of contact dermatitis due to zinc chromate from the appearance of the lesions. I asked him about contacts at work. I agree with Dr Hall's remarks.

DR STANLEY CHAMBERS I was impressed with the same points brought out by Dr Hall. One frequently sees this particular clinical picture, a dermatitis from zinc chromate superimposed on a seborrheic background.

DR H C L LINDSAY This is psoriasis of a seborrheic type. If it were a chromate dermatitis, it would continue as long as the man keeps working, and he says that it comes in the winter and goes away in the summer.

DR PAUL FOSTER This man has an eruption which on his first visit to the office I considered to be seborrheic dermatitis, but as nothing that has been done has helped him at all, I am not so sure about the diagnosis. It is worthy of note that this man is particularly free of seborrheic dermatitis of the scalp, and I have never seen him at any time when he had a seborrhea of the scalp. At one time he had an eruption in the axilla which I considered to be a seborrheic dermatitis. He still has that lesion, and it has not improved with any form of therapy. He has had at least twelve roentgen treatments. Salicylic acid and sulfur ointment, ammoniated mercury and tar ointment have been used locally. There has been no improvement. It is my first case of seborrheic dermatitis, if that is the diagnosis, that has not responded to some of these forms of treatment. The biopsy is not suggestive of a premycotic mycosis fungoides or lymphoblastoma. I appreciate the discussion, especially Dr Hall's remarks as regards the resins used in the airplane industry. I shall test the patient's tolerance to zinc chromate and other paint resins and report at a later meeting.

NOTE—A strong positive reaction to a patch test with zinc chromate was reported for this patient by Dr Foster at the next meeting.

# MANHATTAN DERMATOLOGIC SOCIETY

ANTHONY C CIPOLLARO, M D, *President*

WILBERT SACHS, M D, *Secretary*

March 14, 1944

## Congenital Cyst of Frontal Bone Presented by DR MAURICE J COSTELLO

J S, a girl 7 months old, was first seen by me on Dec 21, 1943, because of a nevus simplex in the sub-occipital region. At a subsequent visit her mother drew attention to a round, solid, bony prominence, the size of a cherry pit, in the region of the inner half of the left eyebrow. When the infant arched her eyebrows, a bony depression, or defect, could be seen just medial to this area.

### DISCUSSION

DR DAVID BLOOM This is a dermoid cyst, which is found most frequently in this region, which corresponds embryologically to the region of the branchial cleft, where developmental disturbances take place.

DR HERMAN SHARLIT Does Dr Bloom mean that these are deposits of cholesterol?

DR DAVID BLOOM No, they are cysts which contain sebaceous glands and hair, and they may contain coil glands also and even teeth.

DR MAX SCHEER Can the diagnosis of osseous cyst be made without a roentgenographic examination? And how can it be differentiated from an osteoma, which I think it is?

DR E WILLIAM ABRAMOWITZ I am inclined to agree with the diagnosis of dermoid cyst. It might be advisable to make roentgenograms of all the bones in order to exclude the presence of other osseous lesions, such as appear in Albright's syndrome and other entities.

DR ANTHONY C CIPOLLARO The lesion involves bone structure, it is either a cyst or an osteoma, rather than an atheroma or a dermoid cyst.

DR MAURICE J COSTELLO I believe that this is a congenital cyst, due to some embryologic defect the nature of which is obscure.

## Scleroderma and Acrosclerosis Presented by DR E WILLIAM ABRAMOWITZ

Mrs B S, a Jewish woman aged 28, was born in the United States. Soon after the birth of her child, about two and a half years ago, she noticed an eruption on her right hand, which has since spread to various parts of her body. She had no previous illnesses.

The patient now presents a definite hidebound condition of the fingers and extending to her elbows and on her face and extending down to the clavicular region shoulders, chest, abdomen, hips, groins and legs. The characteristics of Raynaud's disease were present last winter and also this year. Her toes are livid.

She has had mecholyl iontophoresis and dihydrotachysterol, with little result. She is presented for suggestions as to further treatment.

### DISCUSSION

DR MAURICE J COSTELLO I agree with the diagnosis. I believe that the acrosclerosis is part of the clinical picture of scleroderma. I suggest that large doses of dihydrotachysterol be administered to this patient.

DR GEORGE M LEWIS To many competent observers, acrosclerosis has not been adequately established as a separate entity.

DR MAX SCHEER I agree with Dr Lewis, that such cases are cases of scleroderma. The acrosclerosis is simply a peculiarity of localization to the extremities.

DR E WILLIAM ABRAMOWITZ There are some unusual features that I should like to consider. The patient looks younger than she actually is. Her hair is prematurely gray. There is hypertrichosis of the arms and legs, and with the sclerodactylia the picture resembles what has been described as Werner's syndrome and points to some endocrine disturbance. The patient has not responded to dihydrotachysterol or mecholyl iontophoresis. She has been studied with every possible means, including electroencephalography, at the vascular clinic of the New York Post-Graduate Medical School and Hospital. I have confidence in the efficacy of massage and baking. As to the word "acrosclerosis," I feel that the term is redundant. Scleroderma and acrosclerosis are probably the same process. As to the question of operating on the parathyroids, I believe that this measure is being abandoned. I am considering sympathectomy to give her relief.

## Tinea Capitis Presented by DR ANTHONY C CIPOLLARO

F D, a boy aged 9, consulted me on Oct 11, 1943 because of an area of baldness in the occipital region, of several weeks' duration. Examination under Wood's light revealed a patch of tinea capitis in the occipital area, about the size of a silver dollar. There was no evidence of fluorescent hairs elsewhere. A culture showed the fungus to be *Microsporon audouinii*. On October 13 the patient was again examined under Wood's light, and there was no evidence of fluorescent hairs except in the patch in the occipital region. A dose of 340 r of low voltage unfiltered roentgen rays was applied to the affected area. This was 12 per cent greater than the dose usually employed, because only a small area of the scalp was being epilated. The area was carefully covered with moleskin adhesive plaster. On October 20 he was again examined under Wood's light, and there were no fluorescent hairs except on the affected areas. On November 3 there were some fluorescent hairs remaining in the occipital region, and several patches of fluorescent hairs were found on other portions of the scalp. He was treated with various topical remedies and by manual epilation until November 26, but the disease became progressively worse.

On November 29 the entire scalp was given an epilating dose of roentgen rays (300 r) with the five point technic of Kienbock and Adamson, and on December 20 there was complete, uniform epilation all over the scalp. The patient has been observed weekly. Various topical remedies have been used, and on Feb 16, 1944 there was still evidence of tinea capitis. Treatment with salicylic and benzoic acids in a penetrating solution was begun.

### DISCUSSION

DR GEORGE M LEWIS First of all, this shows the bad results sometimes obtained by treating one part of the scalp. The technic which Miss Hopper and I have recently published (Lewis, G M, and Hopper, M E Ringworm of Scalp, Successful Use of Roentgen Rays to Epilate Local Areas of Infection ARCH DERMAT & SYPH 49 107 [Feb] 1944) is often successful, but one runs the risk of just this sort of result. We still think it is worth while in selected cases, particularly

for older children with no recent spread. We now keep the scalp covered with grease between the time of epilation and shedding of the hair and prohibit washing of the scalp during these three weeks. A little grease is applied every day, and the area is kept covered with cellophane or wax paper and a stockinet headpiece. I admire the courage of Dr. Cipollaro in giving a second treatment with roentgen rays for epilation six weeks after the first treatment. I still lean toward conservatism and believe that six months should elapse between epilations. The hair has apparently been stimulated at the site of the two epilations, and this is worthy of further study.

**DR MAURICE J. COSTELLO** The result obtained by Dr. Cipollaro in this case is paradoxical. It is nevertheless interesting and may be significant. I have seen this type of regrowth in patches formerly affected by fungous infection. It is a fairly common experience after epilation to find stimulation of growth in patches formerly affected by tinea, the hairs in these patches grow faster and are stronger than in those areas not similarly affected. The regrowth in this case occurred in a patch formerly involved by tinea capitis.

**DR ANTHONY C. CIPOLLARO** This is the most interesting phenomenon I have ever encountered in radiology. Two epilating doses of roentgen rays applied to the occipital area with an interval of six weeks between doses produced an apparent increase in growth of hair on that portion receiving the larger dose. It is also interesting to note that 600 r applied in two sittings with an interval of six weeks did not prevent regrowth of hair. I have no explanation for this unusual occurrence.

**A Case for Diagnosis (Chronic Lymphangitis, Rhinoscleroma?)** Presented by **DR E. WILLIAM ABRAMOWITZ**

**A. J.** a white woman 32 years old, was born in the United States but lived in the West Indies for several years when a child. She is subject to yearly streptococcal infections of the throat, although her tonsils were removed at the age of 6. She first noticed a discharge from lumps on the sides of her nose about fifteen years ago. Thereafter she noticed that the skin on the bridge of the nose had hardened. Ever since that time the patient has been subject to attacks of redness on the bridge of her nose every other day. The rhinologist reported an infected sinus which was treated with a sulfonamide compound in solution and sprays. There has been some improvement in the nasal cavity but not in the appearance of the cutaneous lesion. The mucous membrane of the nasal cavity shows no sign of sclerosis.

**DISCUSSION**

**DR GEORGE M. LEWIS** This is a difficult case to discuss from the point of view of exact diagnosis. The cultures have not yet been reported. A biopsy would be of interest if Dr. Abramowitz could get one.

**DR MAURICE J. COSTELLO** I think that this eruption is due to chronic lymph stasis, possibly dating from the time that the patient had an operation on her nose. It is commonly referred to as solid edema.

**DR HERMAN SHARLIT** I agree with Dr. Costello.

**DR WILBERT SACHS** I agree with the diagnosis of lymphangitis, because if the disease were rhinoscleroma there would be considerable changes in the nose and mucous membranes.

**DR E. WILLIAM ABRAMOWITZ** The patient lived in the South American area, and rhinoscleroma is endemic in San Salvador. The rhinologist says the nasal condition has improved. I am inclined to agree with the members that the diagnosis should probably be lymphangitis, but I feel that I should make a smear to rule out rhinoscleroma, as the tissues over the nose are hard to the touch.

**Recurrent Erythema Multiforme Confined to One Finger** Presented by **DR GEORGE M. LEWIS**

**S. K.**, a man aged 44, was first seen on Dec. 28, 1943, while he was in New York Hospital, under the care of Dr. Gardner Childs, for treatment of an infection secondary to his cutaneous lesion.

According to his history, the patient has had a lesion at the same site on the right index finger once, sometimes twice, a year for the past ten years. There is always an associated lymphangitis and frequently a high fever. The attacks last about one week. They usually occur in December but occasionally in the spring as well. The lesions appear as erythematous circinate elevations surmounted by a bulla. On March 9 the patient became aware of a beginning lesion. He was given 0.5 Gm. of sulfathiazole internally three times a day.

**DISCUSSION**

**DR MAX SCHLER** I agree with Dr. Rosen that this is recurrent erysipelas.

**DR E. WILLIAM ABRAMOWITZ** I should also be inclined to exclude erythema multiforme. Dr. Lewis states that the lesion subsided under treatment with a sulfonamide compound, and this fact is in favor of a possible erysipelatos infection.

**DR MAURICE J. COSTELLO** I should like to suggest to Dr. Lewis the possibility of the diagnosis of herpes simplex. Patients have been presented before this Society with this eruption on the terminal phalanges, recurring two or three times a year. It might be interesting the next time this eruption recurs to scrape some of the vesicular fluid into the cornea of a rabbit. Recurrence in 1 of the reported patients was prevented only by the administration of a sulfonamide compound given at the beginning of an attack.

**DR HERMAN SHARLIT** I think that Dr. Lewis' judgments carry a consistent type of medical reasoning, and I believe that physicians have seen more and more diseases which are infectious and episodic that can be inhibited or cured. As to the locations in which herpes simplex occurs most frequently, the hands are second to the face. If the sulfonamide compounds can inactivate and abort such lesions, they should be employed.

**DR GEORGE M. LEWIS** The lesion which I saw in December was a typical iris lesion, and no one would consider any other diagnosis than erythema multiforme. The absence of a history of ingestion of drugs, the fact that the lesion is of a fixed type and the presence of infected tonsils are pertinent points. There was never any indication of herpes simplex in this lesion seen tonight or in the former lesion, and from a close questioning of the patient there is nothing to suggest that diagnosis in prior attacks.

**Acrodermatitis Perstans of Hallopeau Treated Successfully with Tyrothricin** Presented by **DR MAURICE J. COSTELLO**

**M. M.**, an Italian plasterer aged 44, lacerated the second, third and fourth fingers of the right hand in



November 1943, when a wine jug broke in his hands. At the sites of the lacerations, which were treated at the time with sulfathiazole powder, circumscribed areas of dermatitis developed, consisting of granulomatous tissue exuding a seropurulent discharge and having a somewhat foul odor. This persisted and progressed in spite of many forms of therapy, including wet dressings of solutions of aluminum acetate, of boric acid and of potassium permanganate and administration of zinc peroxide and roentgen rays.

On Feb 16, 1944, after the application of the electric cautery to one of the pyogenic-granuloma-like masses on the tip of the third finger, a dressing of 5 per cent sulfathiazole ointment was applied. In twenty-four hours there was intense edema and vesicular dermatitis involving this finger and the dorsum of the right hand. His family physician, thinking that the patient had acquired a superimposed streptococcal infection, administered one dose of sodium sulfadiazine intravenously to the patient. Within several hours fever, headache and a generalized, discrete papulovesicular eruption developed, which was more evident on the exposed areas of the body, especially on the forehead, face and neck above the collar line. There was a linear area of vesiculation on the left cubital space, where a band of adhesive tape had been applied after the injection had been given. One may assume that there had been leakage of the drug from the syringe. A roentgenogram of the fingers of the right hand on February 28, showed no osseous changes. About March 1 the patient began to apply wet dressings of tyrothricin (Squibb), which contains gramicidin and tyrocidin in water. The solution was made up of 1 part tyrothricin and 4 parts isotonic solution of sodium chloride. Immediate improvement followed.

#### DISCUSSION

DR E WILLIAM ABRAMOWITZ I think that splendid results are obtained with this new antibiotic. I had a chance to use tyrothricin in a case of varicose ulcer secondarily infected, with apparently good results.

DR GEORGE M LEWIS I am glad to know about this case, and, since this disease is most recalcitrant to treat, I shall certainly try this form of therapy for other patients.

DR MAURICE J COSTELLO I thought that this patient had acrodermatitis perstans, because he had an injury followed by infections that were persistent and resistant to all forms of treatment. Three days after the patient received tyrothricin, the eruption began to improve.

#### **Mycosis Fungoides** Presented by DR ANTHONY C CIPOLLARO

F B, a man aged 54, was previously presented before this Society on April 12, 1938 (ARCH DERMAT & SYPH 38 636 [Oct] 1938). The patient is re-presented because of the development of painful lesions on the soles, which have interfered with his walking, and also for suggestions as to therapy.

The eruption on the right sole has bothered him for several months. The lesion is scaly and slightly exudative and the edges are somewhat infiltrated. The eruption has not been getting progressively worse, but there have been periods of remission and exacerbation. The patient still has a few scattered infiltrated plaques arranged in circles and portions of circles.

Biopsy performed on April 28, 1938, showed a superficial dermatitis. A recent hematologic study by Dr Rosenthal showed no abnormalities, and a recent complete physical examination, including laboratory studies by Dr Rosenthal and Dr Rubenstein, Philadelphia, revealed normal conditions.

#### DISCUSSION

DR HERMAN SHARLIT I feel that the lesion on the sole has an unusual appearance for any variation of mycosis fungoides, and one would have to inspect it under the microscope for suggestions as to what else it might be.

DR MAURICE J COSTELLO I agree with the diagnosis of mycosis fungoides, but there is one thing missing. The patient has no pruritus whatsoever.

DR GEORGE M LEWIS The fact that the lesions disappear in the summer in sunlight makes one question whether the disease is mycosis fungoides, especially since the histologic observations do not confirm the diagnosis. I am not at all certain about the lesions on the foot. A culture might be important.

DR DAVID BLOOM Some lesions resemble mycosis fungoides, others, psoriasis. I think that it is important to establish definitely the diagnosis, and I advise another biopsy. If it is mycosis fungoides, one would be justified in giving roentgen ray treatment as often as necessary, while psoriasis should be treated in other ways.

DR WILBERT SACHS Tonight I should not make a diagnosis of mycosis fungoides, because of the clinical appearance of the lesions, because they do not itch and because they go away with ultraviolet as well as roentgen irradiation. Yet I cannot help recalling those patients of Dr Chargin's who he insisted had mycosis fungoides. Many biopsies were performed, none showing mycosis fungoides, until finally in 1 patient a definite picture of that disease developed. It would not surprise me if this patient finally showed typical mycosis fungoides.

DR E WILLIAM ABRAMOWITZ It is known that cases have been reported in which psoriasis was present for many years, and then the mycosis fungoides developed. Just now some of the lesions resemble psoriasis nodularis. Itching is not necessary in mycosis fungoides. The lesion on the foot can be considered as part of the picture. Bullous lesions have been described in mycosis fungoides. There is a possibility of malignancy.

DR ANTHONY C CIPOLLARO An ordinary case of mycosis fungoides would not have been interesting. I presented this patient because he has lesions resembling those of other diseases. When he was first presented, he had a few lesions more typical of those of mycosis fungoides than those present tonight. There were definite ulcerative lesions arranged in semicircular form and round plaques of various sizes. The members agreed then that it was a typical case of mycosis fungoides, in spite of the fact that biopsy did not then confirm the diagnosis. I have watched the patient and am finally convinced that hers is a mild form of the disease, kept under control by ultraviolet irradiation and roentgen rays, and that the lesions on the sole are of the bullous type of mycosis fungoides. I shall perform a culture to determine whether there is a fungous infection, although I personally do not believe there is. NOTE—A biopsy showed mycosis fungoides.

## CHICAGO DERMATOLOGICAL SOCIETY

L M WIEDER, M D, *President*MARCUS R CARO, M D, *Secretary*

March 15, 1944

**Acanthosis Nigricans, Juvenile Type** Presented (by invitation) by DR S ROTHMAN and DR A L SHAPIRO

H A, a girl aged 15, first noted darkening of the skin on the nape of the neck about three years ago. Since then, similar lesions have appeared on the upper part of the back, in both axillas, in the intermammary region and on the thighs and perineum.

She has been overweight and tall all her life. Her intelligence has always been above normal. Menstruation began at the age of twelve and has always been normal. The administration of thyroid had no effect on obesity or cutaneous changes.

The father (aged 47) has diabetes. The mother (aged 36) is obese but otherwise healthy. There are two normal siblings.

A physical examination revealed no organic disease except the cutaneous lesions and a "buffalo" type of obesity. The weight is 220 pounds (99.8 Kg) and the height is 68 inches (173 cm). The blood pressure at rest is 126 systolic and 98 diastolic.

The cutaneous lesions consist of plaques of papillary hypertrophy and pigmentation in the locations mentioned previously. Papillomas are present within these areas. Striae are present on the abdomen. There are mild acne and some roughening of the cheeks.

The dopa reaction was weakly positive. The silver stain revealed definite hyperpigmentation.

Examination of the urine and blood revealed no pathologic changes. The basal metabolic rate was determined on several occasions and was between -18 and -21 per cent. The dextrose tolerance test in 1943 revealed decreased tolerance (fasting value 110 mg per hundred cubic centimeters, one-half hour value 190 mg, one hour value 190 mg, two hour value 110 mg and three hour value 90 mg), in 1944 the tolerance was within normal limits. No glycosuria was observed during these tests. The blood cholesterol level was 230 mg per hundred cubic centimeters in 1943 and 180 mg in 1944 (within normal limits). The whole blood of the patient was tested for the presence of melanophore hormone by the hypophysectomized frog method, this test yielded a negative result.

The roentgenographic examination of the skull revealed normal bones and sella turcica, that of the left wrist showed premature closing of the distal radial epiphyses.

## DISCUSSION

DR S W BECKER I believe that this is a typical example of the juvenile type of acanthosis nigricans. The girl is obese, a condition which is usually found in association with this disease. She has always been obese, and the mother is also overweight. This girl does not present any abnormality in sugar tolerance, but often such changes are not found.

DR THEODORE CORNBLEET It can be assumed that probably the chromaffin system is the site for development of the phenomena present here, whether through the pressure of tissue incident to corpulency or from a new growth. On the chance that the latter is the case, it would be well to continue watching this patient.

DR S ROTHMAN (by invitation) Reviewing the literature, one finds that in the majority of cases of this type the tolerance for dextrose is just at the border line of pathologic decrease. Sometimes there is alimentary glycosuria, but there is no true diabetes. It is striking how much the patients look alike. In the juvenile form, malignant neoplasms have never been found. Three cases were reported, however, in which 1 of the parents died early from carcinoma (ARCH DERMAT & SYPH 48 468 [Oct] 1943).

The opinion of the endocrinologists is that it is impossible to investigate this disease from any angle of endocrinology. Probably a growth-promoting factor is present, which is formed in malignant tumors as well as by some anomaly of the pituitary gland. In both cases this factor may lead to the same type of epidermal hyperplasia.

**Tuberculosis Miliaris Disseminata Faciei** Presented (by invitation) by DR MAURICE OPPENHEIM and DR DAVID COHEN

J M, a white woman aged 24, had always been in good health except for having acne vulgaris of the face for a short time. About the middle of November 1943 nodules appeared, and in two weeks they covered the entire face. Since that time, only a few new nodules have appeared on the neck and face, particularly on the lateral mandibular areas. The lesions caused itching during the developmental stage.

Almost the entire face is covered by round red-brown and brown nodules ranging from the size of a hempseed to that of a pea. The consistency of the nodules is soft. An impression made with the end of a probe remains as a little dell. The lesions are grouped about the lids and in other areas. On diascopic pressure they present an apple-jelly-like yellowish brown color. There are no scales or crusts on the top. A few of the nodules have a yellow point in the center. There is mild itching. No confluence is present.

The histologic examination showed epithelioid tubercles with few giant cells and lymphocytic infiltration around and on some areas of necrosis.

The general physical examination revealed no abnormalities. The blood and urine were normal.

## DISCUSSION

DR H E MICHELSON, Minneapolis This particular form of cutaneous tuberculosis is rare, even though it is often included in the discussions. I think that the members realize that few examples of true tuberculosis miliaris disseminata faciei have been exhibited. The disease was recognized by the early French and German writers, and Arndt wrote a splendid article some twenty-five years ago. Since then, the publication of Peck gives the latest contributions. Clinically, the characteristics are miniature, discrete, deep-seated lupous papules which are elevated above the surface of the skin. They do not form plaques. They often occur on the lower eyelids and the upper lip but, strangely, are not associated with lesions elsewhere. Each lesion runs its own course, hence lesions in all stages from incipency through scarring are present after the disease is well established. Even though there may be softening in the center, there is no crusting, and the lesions heal without sloughing. Most of the labile forms of cutaneous tuberculosis occur in crops, and recurrence is the rule, but in cases of tuberculosis miliaris disseminata I have never seen recurrence. In spite of the fact that most authors claim a characteristic histologic pattern with central caseation necrosis, my experience



has taught me that this characteristic is by no means consistently present. There has been much discussion of the proper classification of this disease. Dr Laymon and I have decided that it possesses all the characteristics of a tuberculid, and we proposed the name "lupoid papular tuberculid." Treatment probably is not necessary, as the patients get well, but it takes a long time, sometimes more than a year. Gold salts seem to help. Use of the microcautery will of course destroy individual lesions, but it does not bring about the local resistance that natural healing does. Healing after cauterization is slow.

DR RUBEN NOMLAND, Iowa City. Miliary sarcoid in Negroes can look a good deal like tuberculosis miliaris disseminata faciei clinically but microscopically will show a definite sarcoid picture.

DR C W FINNERUD. I should like to ask Dr Oppenheim about the relative frequency of this type of tuberculosis in Austria. I was impressed by the fact that it was actually common in Kren's, Kyrle's, Riehl's Artz's and Oppenheim's clinics. I have seen very few cases in the United States.

DR S ROTHMAN (by invitation). In a patient under my observation (*Zentralbl f Haut- u Geschlechtskr* 20 544, 1926), the lesions were stable and remained unchanged for five to six years. They could be completely destroyed by cauterization so as not to recur. I agree with Dr Michelson that the absence of relapses in loco distinguishes this disease sharply from lupus vulgaris. Tuberculosis miliaris disseminata is torpid, like sarcoid.

DR MAURICE OPPENHEIM (by invitation). In Vienna and Austria there are many more cases of this type than there are here. I have seen only 1 case in Chicago previously.

I read the paper of Laymon and Michelson and I believe that they are right when they stress that tuberculosis miliaris disseminata lies between lupus vulgaris and papulonecrotic tuberculid. Dr Michelson introduced the name of miliary papular tuberculid. Kaposi first described this clinical picture under the name of "acne telangiectodes," because the nodules showed yellow points in the center. These yellow points correspond histologically to central caseation, hence, a typical tubercle gives the clinical picture, and the disease was called lupus folliculosis disseminatus. But there was no connection with the follicles, hence, the final name was set as tuberculosis miliaris disseminata. I should say that the nodules clinically look much like the nodules of lupus vulgaris.

In differential diagnosis differentiation is to be made from sarcoid of Boeck and nodular syphilis. But both of these diseases lack the so-called probe pressure symptom. If one makes an impression with the point of a probe the dell stays a long time in a lupous nodule. In lesions of sarcoid and of syphilis, in which the infiltration is much more intense, either it is impossible to make an impression or the dell is immediately flattened out. One can see in some nodules a little yellow point, and this yellow point means caseation. I am sorry that in the presentation made today the histologic specimen was not very good, but one can see epithelioid tubercles with a few giant cells.

Regarding therapy, I agree with Dr Michelson that there are almost no recurrences after treatment, and that the involution of these nodules is gradual. I observed this woman for two weeks, and I saw some of the nodules disappear. My treatment in this case consists of acetarsone. In my experience the phenylarsones

have an influence on tuberculosis of the skin and also on lupus erythematosus.

#### A Case for Diagnosis (Pemphigus?) Presented by DR MAURICE DORNE

Mrs M P, aged 60, first noticed a bald spot on the top of the head in October 1940. She applied iodine, and after the application vesicles and bullae appeared at the site and on the body. She was treated, and about one and one-half years ago the lesions disappeared. Six months later similar lesions appeared in the mouth and on the lips after the extraction of her teeth. She was treated with various local applications and with injections and, prior to consulting me, had received about ten roentgen ray treatments to the lips.

An examination revealed a dollar-sized erythematous atrophic patch on the vertex of the scalp and numerous pigmented and depigmented patches on the shoulders, arms, scapular regions and back. The skin is dry. The greater portion of the lips are covered with crusted, verrucous-like patches. There is a single bulla on the hard palate and another on the under surface of the tongue.

The Kahn reaction of the blood was negative. Results of examination of the peripheral blood were as follows: hemoglobin content, 82 per cent, erythrocytes, 3,780,000, and leukocytes, 10,000, with a differential distribution of 68 per cent neutrophils, 8 per cent eosinophils, 30 per cent lymphocytes, 1 per cent basophils and 1 per cent monocytes.

#### DISCUSSION

DR M H EBERT. Clinically, when I first looked at this patient I thought she had an extensive cheilitis glandularis apostematosa with crusting. When I had her open her mouth and looked back at the mucosa, I could see vesicles and bullae on the posterior surface of the hard palate and pharynx and similar lesions on the buccal mucosa. She had some reddening of the scalp, but that was nonspecific clinically. Then I read the history and found that she has had multiple bullae on the skin as well as in the mouth. From the history of the first lesion in the scalp, which appeared after the application of tincture of iodine, I believe that it seems to fulfil Dr Oppenheim's criteria for the primary lesion of pemphigus vulgaris. I agree with the diagnosis that it is a case of pemphigus vulgaris.

DR C W FINNERUD. I first saw this patient at the time of her first attack several years ago. According to the history she gave at that time, she had a bullous lesion on the scalp which she repeatedly painted with tincture of iodine. Thereafter, bullous lesions in general distribution developed in the mouth. She was given an arsenical and large doses of vitamin D, which within a few months cleared the lesions completely. I understand that she remained free of lesions up to the time of the present attack. I thought that she had pemphigus.

DR JAMES H MITCHELL. Dr Scull and I had this patient under observation all last year. We never presented her case because we never knew what her disease was.

DR RALPH H SCULL. The specimen for the biopsy that I made, when she was a patient at Rush Medical College, was prepared by the general pathologic department and, unfortunately, it had been cut in the wrong direction. However, the changes were those of a banal type of infiltrate. There was nothing observed that would lead one to think of pemphigus as a diagnosis.

DR M H EBERT When you first saw the patient, were the lesions on the lips the striking feature, as they are today?

DR JAMES H MITCHELL Not nearly so striking I have a colored picture that I made a year ago At that time the lesions on the scalp and on the lips made us consider lupus erythematosus, but we never arrived at a differential diagnosis

DR MAURICE OPPENHEIM (by invitation) In this case one has a typical example of a primary lesion in chronic pemphigus (Oppenheim, O M, and Cohen, D Primary Lesions of Pemphigus Vulgaris, ARCH DERMAT & SYPH 46 201-206 [Aug] 1942) Four years ago the patient had crusted lesions on the scalp which healed after a rather long time with a scar and with loss of hair After a long interval, the generalized bullous rash appeared The scalp is a typical location for a primary lesion of pemphigus Others are the mucous membrane of the mouth and the umbilicus If the primary lesion is located in the mouth, the prognosis is bad, because usually this is the initial symptom of pemphigus vegetans Primary lesions of pemphigus during recent years were observed by M J White, Oliver, Ebert, Zakon and others

DR CLINTON W LANE, St Louis It is with hesitancy that the following remarks are made, in view of the much longer period in which this patient has been observed by other dermatologists However, the patient stated to me that the initial symptom on the scalp was baldness To the bald patch, tincture of iodine was applied, after this, blisters appeared for the first time With the history and, the presence of an atrophic, irregular, diffuse and faint erythematous area of alopecia, a diagnosis of pseudopelade in the early stage is suggested

DR MAURICE DORNE I originally thought that the clinical findings were consistent with pemphigus and therefore instituted treatment with acetarsone administered orally The duration of treatment has not been sufficient to permit any definite conclusions, but the lesion on the lips had shown a noticeable improvement and then became worse again while under treatment

**Hyperpigmentation of Abdomen (Von Giercke's Disease, Hyperinsulinism?)** Presented by DR THEODORE CORNBLEET and (by invitation) DR HENRY C SCHORR

L C, a married white woman aged 30, about four years ago observed discoloration on her abdomen simultaneously with the occurrence of pains in the right upper quadrant and the epigastrium The following year, she was operated on for a tumor mass in the epigastrium, which was found to be due to an enlarged liver Biopsy of the liver showed abnormal deposits of glycogen In January of this year she was again observed, because of recurrence of the pains in the right upper quadrant of the abdomen and epigastrium and nausea and vomiting A blood sugar tolerance curve was found to be abnormally flat, and, after a study of the various laboratory data and physical examinations, it was thought that the proper diagnosis was hyperinsulinism All the laboratory data were more or less within the normal ranges for the various tests made The leukocyte count was 13,300 The blood sugar tolerance curves were definitely abnormal The diastase test on the blood showed 64 units (upper normal is 32) The fasting blood sugar level was 100 mg per hundred cubic centimeters

The examination of the skin shows the abdomen to be diffusely pigmented as far as the the thorax and down to the groins

## DISCUSSION

DR THEODORE CORNBLEET Von Giercke's disease is clinically characterized by hepatomegaly and enlargement of the heart and, occasionally, of the kidneys (almost exclusively in children) It is anatomically characterized by deposition of glycogen in the liver, spleen and heart muscle Glycogen in the tissues is quickly destroyed by the diastatic enzymes present, which leads to the formation of sugars Functionally, von Giercke's disease is characterized by the inability of diastase enzyme to split glycogen, which, in turn, leads to enlargement of the organs

Biopsy specimen from this woman's liver was found filled with glycogen On this account, von Giercke's disease was thought to be a possibility Other possibilities suggested were tumor of the pancreas and hyperinsulinism Speaking in favor of the latter hypothesis were two episodes of hypoglycemic shock The dextrose tolerance curve was flat, and this was exaggerated in the double dextrose tolerance curve, which evidence supported the diagnosis further In any event, some enlargement of the abdominal viscera probably is producing pressure on chromaffin structures Fibrosis without actual tumor formation has been seen to give rise to pigmentary phenomena The mechanism whereby these abdominal changes induce pigmentation is of course unknown This patient is to be operated on shortly, and it is hoped that this will clarify the situation

**A Case for Diagnosis (Lichen Sclerosus et Atrophicus, Morphea?)** Presented by DR J H MITCHELL and DR R H SCULL

M K, a white girl aged 9 years, presents an eruption that has been present for two years The mother states that the skin of the right shoulder was first involved and healed spontaneously Later, lesions appeared on the face and scalp

On examination, there is a more or less linear pigmented depressed scar near the right shoulder blade On the right side of the face, there are slightly elevated bluish lesions intermingled with some white faded areas

The laboratory reports on blood and urine revealed no abnormalities

The biopsy of a specimen from one of the areas of the scalp showed a thinning of the epithelium with obliterations of the rete pegs The subepithelial layer showed a homogenization of the collagenous fibers Deep in the corium, there was a round cell perifollicular infiltrate

## DISCUSSION

DR F E SENEAR I thought of the possibility of the patient's having lichen sclerosus or morphea It seemed that the atrophy was not as whitish as is seen in lichen sclerosus Clinically it was closer to morphea, especially with the hematophy in that location

DR RALPH H SCULL (demonstrating the section) There is an almost complete obliteration of the rete pegs The subepithelial fibers are compressed There is a round cell perifollicular infiltrate The section taken from the part that was bluish showed only a thinning of the epithelium

DR LOUIE H WINER, Minneapolis There is no distinct homogenization of the upper part of the cutis papillaris such as one finds in lichen sclerosus et atrophicus Also, there is not the bandlike lymphocytic

infiltration shown beneath this homogenized area that is typical of lichen sclerosus. There is an infiltrate around the vessels such as is seen in morphea. This type of infiltration occurs with enlargement of the individual fibers, as Dr Scull mentioned. I favor a diagnosis of morphea.

DR R H SCULL. Considering the clinical and histologic picture, we favored the diagnosis of circumscribed scleroderma.

#### Von Recklinghausen's Disease Presented by DR M H EBERT and (by invitation) DR M OTSUKA

M K, a Negro girl aged 16, presents cutaneous changes of various types: (1) deep chocolate-colored macules of varying size which are darker than the surrounding skin and scattered over the trunk, including a large area over the sacrum, (2) soft, compressible cutaneous tumors which can be invaginated, (3) a great number of subcutaneous nodules varying in size from that of a buckshot to that of a crabapple (these are spherical or spindle shaped, firm and movable, and some of the larger ones are tender), (4) a soft, doughy tumor on the right side of the forehead extending from the glabella to the hair line, (5) mottled bluish pigmentation of the sclera of both eyes and also of the palpebral conjunctiva of the right lower lid, (6) a movable mass the size of a hazelnut in the parotid region of both sides.

On examination the eyegrounds were normal. Roentgenographic examination of the skull, the long bones, the ribs and the chest disclosed no abnormalities.

The mother is living and accompanies the girl. Both are of average intelligence for their social status. The father is dead of an unknown cause. He is said to have had "bumps" on his body. The mother gave birth to ten children. All died in infancy except three. The oldest child, now 31 years old, had a hemiplegia on the left side when 10 years old. The other living brother is in the United States Army.

#### DISCUSSION

LIEUT COL EVERETT R SEALE, MC, AUS (by invitation). This is a rather unusual case. The lesions are deeper than are usually seen. There are few on the surface of the skin.

DR M H EBERT. I consider this to be an unusual variety of von Recklinghausen's disease. This patient presents multiple subcutaneous tumors about the nerves, some of which are definitely tender on palpation. The boggy mass over the right eyebrow is sometimes called a cirroid lesion by neuropathologists. They consider it a diffuse involvement of the nerves of the corium. It is curious that the mass always occurs over one or the other half of the brow, as it has done in this case.

There was nothing unusual about the sections. The silver impregnation methods demonstrated few nerve fibers in the lesion. At one time there was much discussion as to the origin of the tissue in such lesions—whether it was connective tissue of neurodermal origin or of ectodermal origin, derived from Schwann's sheath. I believe at present the general opinion is that the tumor is a mixture of these two types of tissues.

#### Hunt's Syndrome Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS

U S, a Jewish cobbler aged 49, was seen for the first time on Feb 26, 1944. He presented a vesicopustular eruption, limited to the left side of the face

and appearing in groups of variable sizes, and an involvement of the buccal surface of the cheek, the soft palate and half of the tongue. The eruption ended abruptly in the center of the face.

The patient returned on March 7, when he presented a paralysis of the involved area which is still present. Since last seen, otic symptoms have developed.

#### DISCUSSION

DR M H EBERT. I have been particularly interested in this type of case. I think that some members will recall that I presented a patient with involvement of the geniculate ganglion in association with Bell's palsy. The patient was a physician and was shown about two years ago (ARCH DERMAT & SYPH 47 464 [Oct] 1943). In the present case, the man complained of pain in the ear but of no particular dizziness or nausea or diminution of hearing on that side, which is sometimes present. He did complain of extreme pain. If it is known that there is involvement of the gasserian ganglion such symptoms offer no trouble in diagnosis. Patients with such symptoms are usually seen by otologists, and papers have appeared about them in the journals of otology and laryngology.

DR S ROTHMAN (by invitation). The most peculiar feature of this case is that the second and third divisions of the fifth nerve are involved at the same time. I never saw herpes zoster with such arrangement. Usually there is isolated involvement of either the second or the third division. Otherwise, there is a complete analogy to the cases which Dr Ebert has presented.

#### Blastomycosis Presented by DR THEODORE CORNBLEET and (by invitation) DR M OTSUKA

W J, a Negro man aged 58, states that nine months ago his entire left foot became painful and swollen. Two weeks later he observed an almond-sized raised pinkish lesion on the lateral aspect of his left leg. This lesion had multiple sinuses from which gelatinous and yellowish pus exuded. He had been working as an oiler in a defense plant for the past year.

The patient states that he had a chancre at the age of 18 but has never received any antisyphilitic treatment.

Physical examination shows that his right pupil is larger than the left, but they both react to light. There is also a mild bilateral cervical adenopathy. His deep reflexes are greatly diminished bilaterally. On the lateral aspect of the left leg just above the external malleolus, there is a lemon-sized ulcer with a verrucous-looking raw base with a well elevated border. On the upper part of the left shin, there is a palm-sized dull red, painful swelling. The left inguinal nodes are slightly swollen and painful to external pressure.

The examination of the blood showed 82 per cent hemoglobin, 4,800,000 erythrocytes and 6,300 leukocytes. The Kahn reaction was negative, and the blood chemistry was essentially normal, as was the urine.

Blastomycotic organisms were found in the sodium hydroxide preparation of the pus.

#### DISCUSSION

DR M J REUTER, Milwaukee. I have had a patient with systemic blastomycosis under observation for about three years. He had a fever, a 40 pound (18.1 Kg) loss of weight, involvement of one knee joint and cutaneous lesions. With massive doses of iodides (450 grains [29.1 Gm] daily) all objective symptoms disappeared, and the patient has now been apparently well for two years.

DR LOUIE H WINER, Minneapolis I want to mention that the histologic section definitely showed blastomycetes

DR C H STUBENRAUCH JR (by invitation) Recently a patient in the medical service at the University of Illinois was seen in consultation by members of the department of dermatology. This man had been coughing for some time and a consolidated area was demonstrable on roentgen examination. He had several follicular pustules on the face. Some of these lesions were surrounded by a peculiar bluish halo, which suggested the possibility of blastomycosis. On microscopic examination of pus from these lesions, typical budding organisms were found in large numbers. Later a large number of these follicular pustules developed on the trunk and extremities. Blastomycetes were demonstrable in all the lesions examined microscopically. At a later date, the fungus was also found in the sputum and in material obtained by puncture of a lung.

DR THEODORE CORNBLEET The original interest in this patient was not confined to the lesion on his leg, which was that of the ordinary kind of localized blastomycosis. When I first saw him, he had, in addition, multiple small abscesses. They made me think of the possibility that they reflected a systemic blastomycosis. On one knee, there is a thickened edematous pigmented area which is almost fluctuant. This is not the knee on which the verrucous lesion is located. That change, too, may represent a systemic blastomycosis. Time will determine this.

#### Cushing's Syndrome Presented (by invitation) by DR S ROTHMAN and DR Z FELSHER

M R, a 23 year old man, was in apparent good health until one year ago, when he began to have rather severe frontal headaches. His weight increased from 190 to 216 pounds (86.2 to 98 Kg), and he noted the development of purplish striae over the hips, thighs and medial aspects of the knees. In the past three months, his face has become more flushed than usual.

In December 1943, a physician told him that he had sugar in the urine and gave him thyroid extract.

The physical examination showed obesity, noticeably flushed face, large purplish striae over the hips, thighs and medial aspects of the knees, single follicular pustules with hyperkeratotic plugs scattered over the trunk and extremities and hypertrichosis at unusual sites, such as the nape of the neck and sacral region. The blood pressure was 160 systolic and 120 diastolic.

Fluoroscopic examination revealed enlargement of the heart to the left.

The patient was admitted to Albert Merritt Billings Hospital yesterday, therefore, only a few laboratory examinations could be made. There was a trace of sugar in the urine, the nonfasting blood sugar level was 84 mg per hundred cubic centimeters, and the blood cholesterol level was 176 mg.

#### DISCUSSION

DR M H EBERT Some years ago, when I published a paper on hypertrophic striae in which I advanced the idea that there was some toxic effect on the elastic tissue, causing changes which made it less resistant to stretching, I received a personal letter from Dr Harvey Cushing telling me about his ideas on the subject and stating that he had made similar observations on patients like those seen today, with Cushing's disease. He was interested that a similar condition on a smaller and milder scale had been noticed in adolescent girls with mild endocrine disturbance.

#### Mycosis Fungoides in a Negro Presented by DR M H EBERT and (by invitation) DR M OTSUKA

G G, a Negro aged 68, five years ago noticed on the right thigh an itching patch which would come and go. In the next two years new lesions gradually appeared on the lower extremities. Itching has always been present. The patient's average weight was 155 pounds (70.3 Kg), but it is now 130 pounds (59 Kg). There has been no significant loss of strength.

There are large plaques of horseshoe and kidney shape, with infiltrated borders and hyperpigmented atrophic centers. The lesions on the thigh are most infiltrated. There is a little general adenopathy. The eyegrounds are normal.

The examination of the blood showed 50 per cent hemoglobin, 3,970,000 erythrocytes and 7,800 leukocytes, with a differential distribution of 74 per cent polymorphonuclears, 20 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. A roentgenogram of the chest showed no abnormalities. The urine and the basal metabolic rate were normal, and the Kahn and Wassermann reactions were negative.

Specimens for biopsy were taken from the infiltrated plaque on the right thigh and from the margin of the superficial lesion on the right scapula. There was some excoriation present in the latter area. The histologic observations were characteristic of mycosis fungoides.

The report on the sternal puncture indicated active granulopoiesis and a shift to the right. The number of plasma cells was definitely increased. Dr Schwartz stated that such changes are nonspecific and are compatible with chronic marrow stimulation. There was a reversal of the normal albumin-globulin ratio in the blood serum.

#### DISCUSSION

DR LOUIE H WINER, Minneapolis I agree with the diagnosis. The tendency of the mycosis fungoides infiltrate (which I think comes from histiocytes) to go on from the histiocyte stage and form plasma cells and phagocytes containing cellular debris was noted in the section and favors the diagnosis of mycosis fungoides. At the same time, the biopsy of the lymph node showed none of the changes found in Hodgkin's disease—that is, none of the replacement phenomena, not even the replacement of lymph follicles by reticulum. Hence, I think that Hodgkin's disease and mycosis fungoides are definitely two different entities.

LIEUT COL EVERETT R SEALE, MC, AUS (by invitation) The whole lymphoblastoma group of diseases is extremely rare in the South. I have never seen mycosis fungoides in a Negro. I think that in Houston every one in town, including the personnel of the clinic, see no more than one person with lymphoblastoma a year.

DR F E SENEAR I should like to say that the young woman with mycosis fungoides whom we presented last month has been given treatment and now, at the end of four weeks, shows striking involution of the lesions and definite improvement.

DR THEODORE CORNBLEET It is advisable to consider the aspects of radiation therapy, such as sites, interval and intensity, that are compatible with the patient's comfort and yet provide for the greatest longevity. These may not be the aspects that induce the most complete disappearance of the lesions in the least time. There have been some observations made of patients with leukemia, for example, which make one believe that these two goals cannot be reached at the same time.

DR M H EBERT This case was presented primarily for two reasons. One was that, as stated, mycosis fun-

goides in the Negro race is rare. This is the third case that we have presented within the last few years. The first 2 had fatal outcomes. The second reason was that in this case there are the classic kidney-shaped lesions that are commonly described. In many cases of mycosis fungoides presented here, these lesions are not present. Sternal puncture was made, and there were no specific observations. A biopsy of the node was also made, with the expectation that there might be an associated Hodgkin's disease.

In regard to the section which was made this morning, which I had not seen, the biopsy specimens were taken from two places: one, the infiltrated border, and the other, a less infiltrated area. In the section which I saw, there was the textbook picture of mycosis fungoides, with cells of all sizes and fungating nuclei and nuclear fragments and everything one would expect to find. I have not examined the other section.

DR LOUIE H WINER, Minneapolis. I simply want to make the point that mycosis fungoides, which is classified as lymphoblastoma from a clinical standpoint, originates from reticulum from a genetic standpoint. Some think that both Hodgkin's disease and mycosis fungoides start from the same place, the reticulum. In mycosis fungoides the reticulum cells form histiocytes, whereas in Hodgkin's disease they go on to form the Sternberg-Reed cells, or giant cells.

DR CLINTON W. LANE, St. Louis. I do not believe that I have seen mycosis fungoides in a Negro patient in St. Louis in the last fifteen years.

#### Leukomelanoderma Following Arsenical Dermatitis (Malignant Melanoma). Presented (by invitation) by DR S. ROTHMAN and DR Z. FELSHER

S. P., a 53 year old man of Greek extraction, was admitted to Albert Merritt Billings Hospital in November 1941 with arsenical dermatitis, damage to the liver and hemorrhagic encephalitis, after treatment elsewhere with neoarsphenamine for latent syphilis. He had received one injection of 0.6 Gm of neoarsphenamine and six injections of 0.9 Gm of neoarsphenamine weekly before the eruption appeared. The dermatitis healed with spotted melanosis and depigmentation. The dopa reaction of the depigmented areas was negative. From February 1942 on, the patient has had courses of intramuscular injections of bismuth subsalicylate in oil at regular intervals. The Wassermann and Kahn reactions became negative in September 1942, but since that time he has occasionally had weakly or doubtfully positive Kahn reactions. The spinal fluid was normal. In August 1943, eighteen months after his arsenical dermatitis cleared, a hard nodule appeared in the left axilla, which grew rapidly. Biopsy revealed a malignant melanoma. The tumor was broadly excised. Roentgenographic examination on Feb. 28, 1944 showed pulmonary metastases. The patient is now receiving roentgen therapy.

#### DISCUSSION

DR S. W. BECKER. I saw this man some years ago, when he first came to the University of Chicago, with exfoliative dermatitis after the administration of neoarsphenamine. There has been a tendency on the part of some writers to confuse leukomelanoderma with vitiligo. The diseases really have nothing in common. The former disease is the result of inflammatory action, and usually the pigment never returns. If patches of vitiligo are treated early enough, there is a possibility of restoration of the melanin. The lymph node which was removed from this patient's axilla shows typical malignant melanoma of the so-called melanosarcoma

type. I examined the part of the body drained by this node and could find no site of a primary lesion. While the patient could not speak English, his interpreter said that he had had no lesion treated which could be interpreted as a primary melanoma. There are only two parts of the body, the skin and the eyes (with the exception of the meninges) where melanoma will originate. It may be that further observation will give more information as to its source. At present I can see no evidence of a primary lesion.

I consider vitiligo to be a functional impairment of the pigment of the skin. I have had several patients who were treated soon after the appearance of the first lesions. I treat such patients as I would any one with a functional disease, in other words, I consider the lesion as a perversion of a sense of fatigue. The regimen includes plenty of rest, generalized ultraviolet irradiation and blistering of the lesion with ultraviolet rays. Often a fair recovery results. After several years the condition seems irreversible.

DR C. W. FINNERUD. Although I am sure that everything as presented is correct, I was wondering whether the pigmented areas had been examined under potassium hydroxide or sodium hydroxide for pityriasis versicolor. I noted that a large amount of fine scales could be scraped off with a dull penknife from those patches.

DR S. ROTHMAN (by invitation). I felt that it was an important question as to whether the malignant melanoma in this case might have originated from the hyperpigmented spots of the leukomelanoderma. Many cases of postarsenical leukomelanoderma were reported, particularly from Germany, in the years between 1920 and 1930, when larger single and total doses of arsphenamine were given than is in the present routine dosage. There is no mention of a single case in which a melanoma had developed subsequently. As Dr. Becker pointed out, the tumor removed from the axilla was a lymph node metastasis. The primary tumor must have been in the skin. In the course of his postarsenical dermatitis, the patient had numerous severe pyogenic lesions, furuncles and hydradenitis, and several of the last-named lesions in the left axilla were incised. Thus, an additional traumatic factor may be considered in the development of the malignant tumor. This patient was one of my subjects in the study on vitiligo (ARCH. DERMAT. & SYPH. 48:400-410 [Oct.] 1943). The white spots were absolutely free of melanin and were dopa negative.

Answering Dr. Finnerud's question, I agree that there has been some scaling, but I did not think of pityriasis versicolor.

#### A Case for Diagnosis (Seborrheic Dermatitis?)

Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. C. SCHORR and DR. DAVID COHEN

S. F., a white man aged 38, has had an eruption on the upper part of his chest and back for two years. The lesions consist of a continuous scaling dry erythema. The affected areas are pale red, and the scale is flaky, comes off easily and is dry, not oily. There is practically no infiltration palpable, and the borders of the lesions are fairly sharply demarcated. There is no itching. Therapy elsewhere has not been successful in removing the eruption.

#### DISCUSSION

LIEUT. COL. EVERETT R. SEALE, M.C., A.U.S. (by invitation). I thought that the patient had seborrhea plus a dermatitis. This is probably one of the most



common lesions seen in the Army in the northern states during the winter. The combination of out-of-doors life, plus dry heat, woolen blankets and woolen clothing is probably the cause. These men always wear woolen underwear, which is irritating. For such dermatitis I formerly used olive oil, hydrous wool fat liquid petrolatum and solution of calcium hydroxide. I now find that solution of calcium hydroxide is satisfactory and much better than olive oil and the solution

**Psoriasis Simulating Stasis Dermatitis** Presented by DR THEODORE CORNBLEET and (by invitation) DR DAVID COHEN and DR H C SCHORR

K B L, a white man aged 46, has had lesions on his right leg for eight years. They consist of sheets of dermatitis which is dark red and scaly. The scales are dry and white and leave pinpoint bleeding when removed. There are no crusts present, and there is practically no itching. A few varicose veins can be seen. Therapy for several years directed toward the improvement of the circulation in the leg has not improved the cutaneous lesions.

DISCUSSION

DR C W FINNLUD: All the lesions are certainly psoriasiform. I think that often there is a tendency to make a diagnosis of psoriasis for a noncrusting eruption of the legs when the disease is some form of stasis dermatitis or neurodermatitis. I feel that if this eruption were not in an area of stasis there would be little evidence of psoriasis. I should hesitate to accept the diagnosis in the absence of lesions of psoriasis elsewhere.

DR THEODORE CORNBLEET: We intended to show a group of 4 patients, each with some unusual variety of psoriasis. Only 1 patient presented himself. When this man was in the Cook County Hospital last year, a biopsy was made. The tissue changes were those of psoriasis. A study group for histopathology was satisfied with this diagnosis. I am embarrassed not to have these slides at hand. Clinically, Auspitz's sign is well displayed. I believe that this man has psoriasis of a kind simulating a chronic stasis dermatitis.

**A Case for Diagnosis (Neurotic Excoriations?)**

Presented by DR JAMES H MITCHELL and DR R H SCULL

M L, a white woman aged 53, has had an eruption for twenty years. She states that it began on the face just before she entered a hospital for an operation. The original lesions began as deep-seated small nodules which would either disappear or come to the surface as red pustules that opened, drained and refilled. Since that time, similar lesions have appeared on the back, chest and thighs. Some would heal spontaneously after a time, leaving depressed round scars. There have been no subjective sensations. The patient's medical history is not significant except for a possible infection of the gallbladder.

On examination there were several erythematous crusting lesions from the size of a pinhead to that of a pea on the back, arms and right hand. There were also a number of depressed scars resulting from previous lesions over a period of years.

On examination the blood and urine were normal. Histologic examination of a specimen from one of the active lesions showed many giant celled tubercles in the corium, consisting of giant cells, round cells, plasma cells and young connective tissue cells.

DISCUSSION

DR H E MICHELSON, Minneapolis: I think that one would have to spend a long time with this patient in order to arrive at a thorough understanding of her and of her eruption. Since she was presented for diagnosis, I felt justified in questioning her at some length, but I was aware that such a "third degree" method might injure her, and I was sorry that I was so persistent. I hope I did not arouse antagonism and resentment in her, which will make future handling more difficult.

The eruption began as an acneform folliculitis, which caused her to excoriate the lesions. She did so through her clothes and often unconsciously, becoming aware of the fact only when she saw blood on her linens. She did not abuse the skin of her face because she was afraid that that would jeopardize her position. (She is a clerk.) The histologic picture is that of a foreign body reaction and might lead one in the wrong direction in making a diagnosis. I think that her eruption should be called neurotic excoriations on a psychic basis. I am interested in the motivations in such persons. Some are purely physical. The patient has, let us say, acne and attempts to improve matters by excoriating the papules or comedos. This act becomes a habit and is continued even to extreme degrees of disfigurement. In order to understand patients whose motive lies in their emotional life, patience, persistence and knowledge of psychic processes are required. The physician must not be pleased with himself when he forces the patient into admission of self production of lesions. The history of such a case begins with the patient's birth, and, if one is interested in the relation between the psychic and the somatic symptoms, much can be elicited from the history. This woman is 1 of 4 children. She was born in Chicago, and she left high school in her second year. She suffered from inadequacy, which was interpreted as physical, and a diagnosis of tuberculosis was made, although no positive evidence was ever found. She went from physician to physician without finding uniformity of opinion, she became discouraged and took up Christian Science. At times, her depression was great. She was unable to work and contemplated suicide but could not go through with it. Then she began to excoriate her skin. Destruction of the skin as seen in dermatitis autophytica, is akin to suicide. The destructive motivation is there. All in all, the facts that I elicited from her seem to point to an emotionally unstable person with depressional tendencies and excoriations produced because of her disappointment in her ability to succeed and the resentment established. I well know that an interview of a few minutes is not conclusive. Such persons need a kindly, supportive psychic therapy, and no "strong arm" threatening admonitions to "stop picking at your skin." I hope that Drs Mitchell and Scull will have a psychiatric report for presentation at a later meeting.

DR LOUIE H WINER, Minneapolis: I diagnosed this eruption from the microscopic section as neurotic excoriations. I have taken biopsies in all my cases, and I find a great many patients have a tubercle-like foreign body reaction deep in the cutis from embedded epidermis, which shows no connection with the more superficial covering epidermis.

DR H E MICHELSON: This woman has had a persistent folliculitis. My interpretation of the slide is a foreign body reaction around the folliculitis in the epidermis. She had vesicles, including some acne-like ones, on the face.

DR S W BECKER I was inclined to think that this eruption might be a tuberculid. The type of patient discussed by Dr Michelson has an unstable protoplasm and allergic diseases will develop in various tissues. The sections do not show the typical characteristics of a tuberculid, but there was a perivascular infiltrate. If the patient had neurotic excoriations, I believe that she would have lesions about the face and other parts of the body.

DR J H MITCHELL We saw this patient last summer, at which time she had lesions which were strongly suggestive of late syphilitic lesions. There were arcuate, annular lesions on the trunk. We discussed it at length with various diagnoses in mind, especially tuberculosis, excoriations and late syphilis. She was given considerable treatment, as I recall. I have not seen her for a long time, but with treatment she made pronounced improvement.

DR RALPH H SCULL We had approached this patient with an open mind, because we had not been able to decide on any type of management. We did not fail to consider the possibility of neurotic excoriations or some other type of lesion by the patient—self mutilation. This patient has cooperated in trying to get cultures of some of the blisters. Many types of cultures were tried.

Two biopsies were made, one of a specimen from an active pustular lesion and one from a healing lesion. Biopsy of the active lesions showed many giant cell tubercles. There were perivascular and perifollicular cellular infiltrates consisting of round cells and leukocytes.

## HAWAII DERMATOLOGICAL SOCIETY.

JAMES T WAYSON, M D, *President* †

HARRY L ARNOLD JR, M D, *Secretary*

*April 8, 1944*

### A Case for Diagnosis (Virus Papillomas in Burn Scars?) Presented by DR HARRY L ARNOLD JR

J R, a 50 year old white business executive, suffered a severe second and third degree burn of the hands, especially the left, on Feb 27, 1944. Many of the nails were lost as a result of it and are regrowing.

Since removal of the petrolatum gauze dressings, a more or less solid growth of hard, dry, horny, yellowish, closely packed papillomas, 1 to 3 mm in diameter, has been observed throughout most of the area of the scar in a streaked pattern. Some of the lesions have been desquamating more or less en masse.

#### DISCUSSION

CAPT DAVID J MUSMAN, M C, A U S I am reminded of similar lesions which I saw a few weeks ago following a gasoline burn in a person with psoriasis. Although the papular element was less prominent, there was considerable hyperkeratosis.

MAJOR GERARD DE OREO, M C, A U S I believe that perhaps the papilliferous appearance is a result of lymphedema occurring coincidentally with healing of the burns. I suggest the use of mild soaks and keratolytic applications.

† Dr Wayson died Jan 17, 1945

### Syphilitic Juxta-Articular Nodules Combined with Leukoderma of Wrists, Palms and Feet Presented by DR HARRY L ARNOLD JR

A L, a 66 year old Chinese-Hawaiian woman, has had nodular growths, 2 to 6 cm in diameter, in the regions of the right elbow and both ankles for about thirty years. They have never been painful or inflamed as far as she can recall. There has been irregular depigmentation about the wrists (chiefly the flexor surfaces) and palms and, to a lesser degree, about the ankles for about the same length of time.

The blood cholesterol level was 210 mg per hundred cubic centimeters (normal). Histologic examination of a section from a nodule on the ankle revealed that it consisted chiefly of collagenous connective tissue, the central part of which was densely homogenized, so that it almost resembled cartilage. There was mild perivascular lymphocytic infiltration about the outer part of the section. The Kolmer, Wassermann and Eagle reactions of the serum were strongly positive (256 Eagle units).

### A Case for Diagnosis (Purpura Annularis Telangiectodes [Majocchi]?) Presented by DR HARRY L ARNOLD JR

H Y, a 27 year old Japanese housewife, was first seen in February 1944 because of an eruption of fifteen years' duration, confined to the legs, chiefly the right. She described the initial lesions as being tiny red spots, first isolated, then grouped and then deeply pigmented.

She presents a profuse eruption, which is a mixture of petechiae, pigmented macules (many of the Cayenne pepper type) and atrophic scars, mostly grouped in dime-sized to quarter-sized areas, there is little tendency toward formation of annuli. There are several early lesions of the same sort on the left ankle. The entire right leg is moderately enlarged and warmer than the left one.

Results of the tourniquet test were negative on both an arm and a leg. The intradermal reaction to moccasin venom, diluted 1:3,000, on both an arm and a leg was negative (pink macules, with no ecchymosis) at one hour. The blood count showed mild hyperchromic anemia and normal white cell and differential counts, there was no eosinophilia. Platelets numbered 185,000 per cubic millimeter of blood. The bleeding time was two minutes, clotting time, four and a half minutes, clot retraction, normal, and prothrombin time, thirty-four seconds (normal). The urine was normal. The Kolmer, Wassermann and Eagle reactions were negative.

Histologic examination of a dime-sized purpuric and pigmented macule of only about two weeks' duration revealed the following picture. Beneath a relatively unaltered epidermis was a profuse polymorphous cellular infiltrate, principally of lymphocytes, eosinophils and neutrophils. These were located chiefly about arterioles, many of which showed hyperplasia of the intima and a narrowed lumen. Considerable yellowish brown pigment, principally phagocytosed, was present.

#### DISCUSSION

DR HARRY L ARNOLD JR I am inclined to feel that the purpura pigmentation and atrophy suggest the diagnosis of purpura annularis telangiectodes, despite the lack of clearcut annulus formation.

LIEUT COMDR M SILVERMAN, M C-V(S), U S N R I agree with the diagnosis as presented. Although the case is not absolutely typical, I have never encountered one that was, and I think that it belongs among the cases of this general category.

DR HAROLD M JOHNSON I suggest the diagnosis of purpuric pigmented lichenoid dermatitis of Gougerot and Blum

CAPT HERBERT LAWRENCE, MC, AUS The histologic changes suggest a granuloma to me I wonder whether leprosy was considered

DR HARRY L ARNOLD JR It was not

CAPT L H ROSENTHAL, MC, AUS I believe that the microscopic picture bears out Dr Johnson's suggestion that the disease is purpuric pigmented lichenoid dermatitis

MAJOR GERARD DE OREO, MC, AUS I think that there are plenty of lichenoid papules, and I am also inclined to classify this case in the group of cases of chronic lichenoid purpura Also, the increased size and warmth of the right leg suggest the possibility of an underlying vascular nevus

CAPT HERBERT LAWRENCE, MC, AUS Can leprosy produce a purpuric picture?

MAJOR EDWIN K CHUNG-HOON, MC, AUS If it does, it must be extremely rare Such a picture has not been seen in Hawaii

**Lupus Vulgaris** Presented by DR HARRY L ARNOLD JR

K S a 55 year old Japanese woman, was first seen in March 1944, because of a lesion of two years' duration on the dorsum of the left forearm This had begun at the edges of a burn scar and had spread slowly

When seen, the lesion consisted of an irregularly oval atrophic scar, about 4 by 6 cm, with a broad, flat, smooth, dull red macule along both its proximal and its distal borders No apple jelly nodules were apparent on diascopic examination The Kolmer, Wassermann and Eagle reactions of the blood were negative There was a 3 plus reaction to a first test strength dose of P P D There was no thermal anesthesia Roentgenograms of the chest showed pleural effusion on the left side Histologic examination showed thickening of the epidermis and a dense infiltrate of lymphocytes, plasma cells, a few epithelioid cells and a few polymorphonuclear neutrophils There were two or three ill defined epithelioid cell tubercles No necrosis was seen No acid-fast bacilli were demonstrated

#### DISCUSSION

MAJOR GERARD DE OREO, MC, AUS I accept the diagnosis and suggest treatment with injections of starch

DR HARRY L ARNOLD JR It is my impression that injections of starch are advocated primarily for patients for whom excision and plastic surgical repair are not feasible I wonder whether for this patient surgical intervention is not preferable

MAJOR SOLOMON GREENBERG, MC, AUS My own experience with injections of starch has not been particularly gratifying I believe that excision and graft are preferable in this case

**A Case for Diagnosis (Psoriasis, Vesicular Lichen Planus, Herpes?)** Presented by DR HARRY L ARNOLD JR

G H, a 29 year old white housewife, was first seen in December 1943, with lesions on the left calf only She stated that these had been present intermittently for a little over two years They were initially blisters, with only one or two appearing at a time, but lately they had become itchy and had been more numerous, flatter and redder than before Each lesion lasted only

a month or so and then healed, leaving no mark, sometimes new ones developed in the same site

Examination revealed a half dozen circular, flat, deep red dime-sized macules within a palm-sized area on the left calf

After two months' treatment the patient had a few new lesions and the old ones were not improved Biopsy revealed at that time extensive formation of superficial vesicles, no eosinophils were noted, the vesicles were multilocular, and the basal cell layer of the epidermis was poorly defined, merging gradually into the cellular infiltrate beneath it No parakeratosis was present Paraffin sections yielded no additional information

#### DISCUSSION

MAJOR GERARD DE OREO, MC, AUS I believe that whatever else the patient has, she has psoriasis of both the scalp and the calves The biopsy strongly suggests herpes simplex and, I think, in combination with the histologic structure, points to a possible explanation of her peculiar history I believe that she may have recurrent herpes simplex, which is eliciting the Kobner phenomenon, so that each herpetic lesion is being followed by a patch of psoriasis, which appears to be pruritic

DR HARRY L ARNOLD JR I am delighted with this convincing and rational explanation of what was to me a completely mysterious picture

LIEUT COMDR M SILVERMAN, MC-V(S), USNR I agree with Major De Oreo's explanation

**A Case for Diagnosis** Presented by DR HAROLD M JOHNSON

C J, a Filipino man aged 35, presents a dollar-sized infiltrated raised plaque on the left angle of his jaw, which has been present for about one year The lesion has not subsided during the last three or four months There has been no tendency toward pruritus, and no other symptoms have been noticed There is no past history of tuberculosis or of any chronic infectious disease, and the patient has felt well during the last five years

The patient was seen on March 2, 1944, at which time he presented an indurated erythematous dollar-sized plaque on the left angle of the jaw No cervical adenopathy was present There was no thermal or tactile anesthesia A tuberculin test elicited a negative reaction Biopsy showed the underlying corium occupied by focal lymphocytic infiltrate concentrated about hair follicles and sweat glands A few epithelioid cells were also present The appearance of the biopsy was nonspecific The Kahn reaction was negative A roentgenogram of the chest was normal

#### DISCUSSION

MAJOR EDWIN K CHUNG-HOON, MC, AUS This patient does not have what are considered the minimum diagnostic criteria for leprosy There is no thermal or tactile anesthesia, there are no demonstrable organisms, and although the great auricular nerves can be seen and felt with ease, they are not nodulated and they do not seem enlarged

DR HAROLD M JOHNSON It occurs to me that this might be lupus erythematosus profundus

**Lichen Nitidus** Presented by DR HAROLD M JOHNSON

J O, a mail carrier aged 26, noticed small lesions ranging in size from that of a pinhead to that of a



millet seed on the dorsum of the index finger of the right hand and a few scattered papules on the dorsum of the fingers on the left hand. They have increased in number but not in size during the last six months. There has not been associated itching or pain. There is no family history of tuberculosis.

The epidermis showed moderate acanthosis. The most striking feature was the presence of four sharply outlined cellular accumulations within the epidermis. These were composed chiefly of lymphocytes, although some epithelioid cells were also present, as well as giant cells. The biopsy was diagnostic of lichen nitidus. Treatment with bismuth subsalicylate has been started, only two injections have been given.

#### DISCUSSION

CAPT L. H. ROSENTHAL, MC, AUS. I suggest the same treatment as is used for lichen planus, the administration of a bismuth compound and an arsenical. The prognosis is good.

LIEUT. COMDR M. SILVERMAN, MC-V(S), USNR. I believe that it is generally felt that this disease is a variant of lichen planus.

#### **Tuberculosis Verrucosa Cutis** Presented by DR HAROLD M. JOHNSON

T. H., a dressmaker aged 34, was accidentally injured fifteen years ago by a foreign object which entered the medial part of her foot. The lesion broke down and drained for several months. It gradually healed, with a slight warty growth remaining at the site of the initial lesion. During the last fifteen years there has been a slow progression of the lesion over the dorsum of the foot. There has been no pain, only a mild itching at times.

Clinically, the patient presents a soft warty verrucous lesion on the base of the right big toe, extending in a linear growth to the dorsum and base of the middle toe. There is also a semiverrucous lesion along the mesial and plantar surface of the foot. A slight erythema at the periphery of the lesion is seen. There are also scars of an old healed lesion. No lesions are demonstrable on any other part of the body.

Biopsy suggested the diagnosis of tuberculosis verrucosa cutis. A roentgenogram of the chest was normal except for a mild hilar thickening, the reaction to a tuberculin patch test was negative. The sedimentation rate was 30 mm in sixty seconds. The Kahn reaction was negative.

#### DISCUSSION

MAJOR GERARD DE OREO, MC, AUS. I suggest treating this patient by thorough curettage, followed by the rubbing of potassium permanganate crystals into the wounds.

CAPT HERBERT LAWRENCE, MC, AUS. Some one suggested the possibility of treatment with injections of starch. I have tried this in a number of cases of this disease, with uniformly unsuccessful results.

#### **Granuloma Annulare** Presented by DR HAROLD M. JOHNSON

M. F., a 55 year old white housewife, presented small pale papules on the dorsum of the left hand and fingers, which had been present for a year and a half. There had been a gradual increase in the size of the lesions. They were later removed surgically and biopsy performed, after which two lesions appeared on the interdigital web on the dorsum of the hand at the base of

the index and middle fingers. There was no pruritus or pain and no other lesions on the rest of the body. There was no family history of tuberculosis or of any chronic infectious disease.

The patient when seen by me had small infiltrated lesions of moderate redness. There was some central involution and peripheral induration of the primary nodules. There were also lesions that were crescentic or ringlike. Roentgen ray therapy had been given by a radiologist for tinea circinata.

Biopsy showed the corium to be occupied by irregular lesions composed of necrotic centers and epithelioid cell peripheries. The peculiar type of coagulation necrosis and arrangement of the cells were diagnostic. The Kahn reaction was negative. A roentgenogram of the chest was normal. A roentgenogram of the spine revealed osteoarthritic spurs.

#### DISCUSSION

The members agreed with the diagnosis as presented. LIEUT. COMDR M. SILVERMAN, MC-V(S), USNR. I suggest the use of solid carbon dioxide with moderate pressure for thirty or forty seconds for the smaller and relatively isolated lesions.

#### **Match Dermatitis on Chest and Secondary and Grease Allergy of Face** Presented by DR HAROLD M. JOHNSON

J. N., a 26 year old man, was first seen on April 7, 1944, with erythematous dermatitis localized on his left and his right breast and a similar dermatitis on his chin, eyelids and ears, present for three weeks. The lesions began six months ago around his left breast, and there was itching and burning in that area. Later a similar lesion developed on his right breast about the size of a palm. There has recently been itching and burning of the chin and ears and upper eyelids. He had been treated by a local physician with injections for a "blood disorder" and also for dermatitis from oil and grease.

A patch test with one of the matches carried in his shirt pocket produced a pronounced reaction.

#### DISCUSSION

The members agreed with the diagnosis as presented.

#### **A Case for Diagnosis (Granuloma Annulare?).** Presented by CAPT HERBERT LAWRENCE, MC, AUS

A young man states that three months ago he noticed for the first time a thickened area of skin on the radial aspect of the distal half of the right index finger. There has been no change in the appearance of the lesion since it first appeared.

The dorsal border of the lesion is parallel with the dorsum of the finger and blends gradually with the normal skin. On the first knuckle of the middle finger of the right hand there is a flesh-colored papule, 5 mm in diameter, which is similar in appearance to the lesion on the index finger except that it does not have the callus-like appearance.

Biopsy was unsatisfactory for histologic study.

#### DISCUSSION

DR HARRY L. ARNOLD JR. My diagnosis is granuloma annulare. I suggest that another biopsy be performed.

DR HAROLD M. JOHNSON. That is my diagnosis, also.

**Melanoma** Presented by LIEUT COMDR M SILVERMAN, MC-V(S), USNR

C A M, a young man, presents a lesion on the side of his nose, which is beginning to show signs of transition from a pigmented mole to a malignant melanoma (nevocarcinoma)

Observation during a hospital stay showed increased activity of the lesion. There has been a recent increase in size, several firm nodules have formed at the upper periphery, and there is a suggestion of activity in the lower periphery

DISCUSSION

LIEUT COMDR M SILVERMAN, MC-V(S), USNR  
This patient is to be sent to Memorial Hospital for the Treatment of Cancer and Allied Diseases, in New York, for definitive treatment

The members agreed with the diagnosis as presented

**Vasomotor Dysfunction Associated with Hypohidrosis** Presented by LIEUT COMDR M SILVERMAN, MC-V(S), USNR

O D K, a young man, gives a history of an acute eruption on the entire body following any simple effort. After ten minutes of exercise there appears on the entire body an erythematous maculopapular eruption. The lesions are discrete and bright red and itch considerably. He also feels exhausted. This condition has been present all his life but has become greatly aggravated during the past three years.

Examination disclosed diminished secretion of the sweat glands. The patient hardly ever perspires on his face, and he sweats but little on his body, except on exertion.

DISCUSSION

The members agreed with the diagnosis as presented

**Gumma of Palate** Presented by LIEUT COMDR M SILVERMAN, MC-V(S), USNR

P D G, a young man, was admitted to the hospital on April 30, 1944, complaining of pain and swelling

involving the anterior right half of the palate and gums. The lesion was opened and the pus evacuated, with amelioration of symptoms. The primary lesion occurred eleven years ago.

DISCUSSION

DR HAROLD M JOHNSON I am not convinced that this was a gumma. The history of onset not long after the extraction of the upper teeth suggests to me the possibility of its having been a foreign body reaction to something introduced at that time.

CAPT L H ROSENTHAL, MC, AUS I am not convinced, either, that this was a gumma.

DR HARRY L ARNOLD JR Was there any evidence of syphilitic osteomyelitis of the palate?

LIEUT COMDR M SILVERMAN, MC-V(S), USNR No, a roentgenogram showed no osseous involvement.

**Granuloma Inguinale** Presented by LIEUT COMDR M SILVERMAN, MC-V(S), USNR

J F H, a young man, was admitted to the hospital on April 2, 1944, complaining of pain, swelling and ulceration of the inguinal area. The lesions started about four years ago. The patient has been in the hospital several times because of sinuses in the groins, perineum and testicles. At present, he shows lymphadenopathy in the right groin and multiple draining sinuses.

The Kahn reaction was negative. Smears were negative for actinomycetes and acid-fast bacilli. No Donovan inclusion bodies were found.

DISCUSSION

CAPT HERBERT LAWRENCE, MC, USA I suggest the possibility of hydradenitis suppurativa.

MAJOR GERARD DE ORO, MC, AUS There were a number of comedos present to support that diagnosis.

LIEUT COMDR M SILVERMAN, MC-V(S), USNR My associates and I have been unable to find Donovan bodies, but we have had only scrapings to examine, not a biopsy specimen.

## News and Comment

### COURSE IN TROPICAL DERMATOLOGY

#### Final Arrangements

As announced previously, a practical course in tropical dermatology will be given in Mexico, D F, Aug 6 to 18, 1945, under the auspices of the Sociedad Mexicana de Dermatologia and the Facultad de Medicina de la Universidad Nacional, México, D F (University of Mexico) and with the cooperation of the Secretaria de Salubridad y Asistencia. This final course has been made up especially for American dermatologists. The subjects listed subsequently will be considered in detail during the two weeks, and the course will include a summary of general information, the presentation of clinical cases and laboratory demonstrations in special fields, such as bacteriology, parasitology, mycology and histopathology.

The Tropical Characteristics of Mexican Dermatology, Dr Jesus Gonzales Urueña, Emeritus Professor of Dermatology, University of Mexico.

Pinta, Dr Salvador Gonzalez Herrejon. General information, late pinta and experimental pinta, results of modern investigations on the cause of the disease.

Onchocerciasis, Dr Manuel Martinez Baez. General information, study of subcutaneous nodules and of cutaneous and ocular lesions, parasitologic study.

Syphilis, Dr Julio Bejarano. Some special characteristics of cutaneous syphilis in Mexico.

Leprosy, Dr Fernando Latapi. General information, the new Brazilian classification of cases and its practical importance, lepromatous (malignant) leprosy, tuberculoid (benign) leprosy and non-characteristic forms, and so-called Lucio's "spotted" leprosy (lazarine leprosy).

Mycosis, Dr Antonio Gonzalez Ochoa. General information, actinomycosis, sporotrichosis, chromomycosis.

Tinea Capitis, Mycologic Data in the Mexican Cases, Dr Antonio Gonzalez Ochoa, Treatment of Tinea Capitis with Thallium Acetate, Dr. Fernando Latapi.

Leishmaniasis, Dr Jorge Millan Gutierrez. General information, presentation of cases, parasitologic study.

Lymphogranuloma Venereum, Dr Oswaldo S. Arias. General information, presentation of cases, the Frei test.

Various medical institutions, including the sections of dermatology of several Mexican hospitals, the Institute of Tropical Medicine, the Leprosy Dispensary, under the direction of Dr Ladislao de la Pascua, and the National Leprosarium, under the direction of Dr Pedro Lopez, will be visited in connection with these subjects. Possibly the town of Iguala, in the state of Guerrero, will be included, so that many cases of pinta can be observed. Other field trips may be arranged, and additional aspects of tropical dermatology may be considered.

For those who do not understand Spanish, arrangements have been made for presentation of all material in

English. A certificate will be presented at the close of this course to each one who has attended the sessions regularly. The fee for this course has been fixed at \$50.

For information and applications, address Dr Fernando Latapi, permanent secretary of the Mexican Dermatologic Society, Zacatecas 220-6, Mexico, D F, Mexico, or Dr Leon Goldman, 733 Carew Tower, Cincinnati 2, Ohio.

Those who have made previous applications are urged to complete their travel arrangements and to make their reservations at the Hotel Geneva, Mexico, D F, at once. Applicants will be notified if any special arrangements for travel are made.

### AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

At the recent meeting of the American Board of Dermatology and Syphilology held in New York city, June 7 to 10, Dr Howard Fox tendered his resignation as president of the Board. Dr Fox had been president of the organization since the Board was first organized, in 1932. Dr C Guy Lane was elected to membership on the Board to take the place of Dr Fox and succeeded him as President.

The following forty-two candidates successfully passed their examination and are now specialists certified by the American Board of Dermatology and Syphilology: Robert Linhart Barton, Surgeon (R), USPHS, Chicago; John Philip Berger, Wichita, Kan; Capt Manuel Gordon Bloom, M R C, USA, Houston, Texas; Martin Vincent Boardman, New York; Arturo L Carrion, San Juan, Puerto Rico; Major Max Harry Cohen, M C, AUS, Augusta, Ga; Garrett Arthur Cooper, Madison, Wis; Capt Frank A Dolce, M C, AUS, Buffalo; Alfred Eliassow, New York; Jerome Kearney Fisher, New York; LaVerne Edward Gaul, Evansville, Ind; Joseph Jacob Hallett, Rochester, N Y; W D Mortimer Harris, New York; Joseph L Hundley, Surgeon (R), USPHS, Jacksonville, Fla; Capt Herbert Henry Johnson, M C, AUS, Swannanoa, N C; Major Frank Jenness Kendrick, M C, AUS, Gary, Ind; George Klein, New York; Capt Herbert Lawrence, M C, AUS, San Francisco; Armond Leo Leibovitz, Surgeon (R), USPHS, Hagerstown, Md; Eugene Lieberthal, Chicago; Max Liebmann, New York; Ludwig W Loewenstein, New York; Donald John McNairy, Surgeon (R), USPHS, Norfolk, Va; Capt Theodore Parker Merrick, M R C, USA, Wilbraham, Mass; Lieut Comdr Donald Strang Mitchell, Montreal, Canada; Grant Morrow, Ann Arbor, Mich; Major Lawrence Meier Nelson, M C, AUS, Omaha; David Vermont Omens, Chicago; Alice E Palmer, Detroit; William Pick, New York; Rees Bynon Rees, San Francisco; Capt Reuben Max Reifler, M C R, USA, Macon, Ga; Frederick Reiss, New York; Lieut Joseph F Ricchiuti (MC), USNR, Pottsville, Pa; Lieut (jg) Edward J Ringrose (MC), USNR, Norman, Okla; Capt Louis Hudson Rosenthal, M C, USA, Detroit; Morris Harris Samitz, Philadelphia; Major Herman Harvey Sawicki, M C, AUS, New York; Francis E Stone, Houston, Texas; Major Orin Milton Stout,

M C, A U S, Los Angeles, George Merritt Stroud III, Cleveland, Lieut Wesley W Wilson, M C, A U S, Tampa, Fla

The following seven candidates successfully passed their examinations and will be certified as specialists on completion of a five year period devoted to graduate training, study and practice restricted to the specialty of dermatology and syphilology: Joseph Gouverneur Gathings, Houston, Texas, John Nathaniel Giekin, Ann Arbor, Mich, Winthrop R Hubler, Cleveland, Arthur Bernard Hyman, New York, Ray O Noojm,

Durham, N C, Julius H Pollock, New York, and Lieut Philip Sneed, M C, A U S, Staten Island, N Y

The time and place of the next examination has not yet been decided. Applications should be sent to the secretary, Dr George M Lewis, 66 East Sixty-Sixth Street, New York 21

## DEATHS

Dr Henry J F Wallhauser died on May 5, 1945

## Book Reviews

**Doctors at War** Edited by Morris Fishbein, M D  
Price \$5 Pp 418, with 82 illustrations New York E P Dutton & Co, Inc, 1945

Armies may successfully prosecute a war without a signal corps, without engineers, without artillery, aviation or cavalry—even without a finance department—but it is said that wars cannot be successfully conducted in the absence of a quartermasters' corps or a medical department. Wars have been lost because of failure of the latter to cope successfully with problems of health of the combatants, failure in transporting of medical supply or in evacuation or inability to combat infection. Until recent years more soldiers died as a result of disease incident to combat than as a result of enemy action.

This book consists of a collection of narratives related by fifteen authoritative medical leaders in the military and naval services and in other agencies responsible for the health of the military and civilian population in wartime. The editor, who in addition to his other duties is Chairman of the Committee on Information of the Division of Medical Sciences of the National Research Council, has written the opening chapter, which contains a succinct consideration of our military medical policy from its development in the early years of the war until it achieved a degree of proficiency hitherto unconceived in this or any other country.

The text is replete with short personal anecdotes of unusual interest, which are sure to appeal to both medical and lay readers. A preamble to each chapter gives a brief biographic sketch of the author, each of whom has been carefully selected on a basis of his ability to present information of genuine value and appeal. Of particular interest is the section on preventive medicine, which relates the various measures taken, to forestall epidemics and maintain proper nutrition of the military personnel. Of no less interest is that chapter on surgery which tells the stories of the control of shock, the use of plasma and blood transfusion, the evacuation of the wounded and the miracles wrought by traumatic and by plastic surgery.

The concluding chapters deal with postwar problems, including what the Veterans Administration has to offer the wounded soldier and a history of the National Research Council, past, present and future. Eighty-two

photographs, charts and diagrams serve to embellish the text. Without exception, this is one of the most interesting and well edited books to emerge from this war.

**The Male Hormone** By Paul de Kruif Cloth  
Price, \$2.50 Pp 243 New York Harcourt, Brace and Company, Inc, 1945

This story, allegedly about testosterone, is an autobiography, written in the breezy, entertaining style of the author. The medical profession has already been treated to a review of this book (*J A M A* 128 316 [May 26] 1945). This reviewer cannot take the "scientific" aspects of the book too seriously. He has been more touched by what has been happening to the author these past few years (male climacteric) and is happy for him that medical science has shown him the way out. We are all happy that this Boswell of hunters in medical science has caught his second wind and that from now on hunting will be more fun than tough "to unearth the skeletons in scientific closets and find out and tell where scientific bodies are buried and report the crimes of character assassination practiced by political doctors."

Surely dermatologists should have a kindly feeling for this chap. Recently, he sent us thousands of cases of dermatophytosis (remember camphor and phenol?). It is quite possible that cardiologists will be the beneficiaries of this story on testosterone.

But seriously, for the moment, I want the author to ponder this. Man's greatest need today is not for more and sustained vital energy but for a strengthening of the ethical and religious directives that will channel human energy toward the goal of a better world. Political economists are ominously hunting of a world revolution that is or is in the making. Nazi Germany revealed, to the astonishment of all, the veneer that is culture on a bestiality that one must sadly confess still possesses man. Into this maelstrom of uncontrolled forces the author wants to throw his "TNT." Unquestionably, most of the testosterone bombs will be duds, but not all.

In spite of this author's huntings, syphilis cannot be cured in one day nor ringworm with camphor and phenol.

# Directory of Dermatologic Societies \*

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Paul A O'Leary, Secretary-General, 102-2d Ave S W,  
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Place New York Time Postponed indefinitely

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S William Becker, Secretary, 55 E Washington St,  
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C E Reyner, Secretary-Treasurer, Henry Ford Hos-  
pital, Detroit  
Place Detroit, 1945

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Henry Abel, Secretary, 339 Union Ave, Elizabeth  
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## CUTANEOUS DISEASES IN THE SOUTH PACIFIC

## OBSERVATIONS AMONG MILITARY FORCES

LIEUTENANT COMMANDER WERNER W DUEMLING, MC-V(S), U S N R

During the past two years it has been my privilege to be attached to a Naval hospital at which large numbers of men returning from the Southwest Pacific have been received for treatment and disposition. A review of the records for the past year reveals that approximately 5 per cent of all admissions to the hospital were to the dermatologic service, and of this number 20 per cent were for fungous diseases of the skin. Of patients seen by me for consultations either from the other services in the hospital or from the outlying Naval and Marine activities to which I am consultant, a diagnosis of fungous disease was made for 20 per cent. Thus, the need for prompt recognition and institution of proper treatment of these diseases is apparent, lest they become epidemic among the enlisted personnel. Although no rare diseases have been encountered, patients returning to the continental United States have exhibited extensive and refractory clinical manifestations, which preclude rapid return to duty under the unfavorable conditions of heat, humidity and filth in the South Pacific areas. This impression has been corroborated by McCarthy.<sup>1</sup>

A close second to the large number of admissions for fungous diseases necessitating evacuation to the United States is the number of admissions for acne of the indurated and cystic variety. It is interesting to note that the incidence of these diseases is the same in both the

tropics and aboard ship. Delaney,<sup>2</sup> reporting from an advance base, listed the incidence of cutaneous diseases in personnel passing through the wards and the outpatient department of the hospital where he was stationed as being as high as 95 per cent and stated that 80 per cent of all personnel had fungous infections if they had served a minimum of three months in the area. Ambler,<sup>3</sup> who was stationed with an Army unit in the South Pacific, observed that the majority of admissions to the hospital were for fungous diseases of the feet and hands. He noted further that acne often assumed the cystic type in that region and that all eczematoid eruptions progressed after arrival, otherwise, the diseases were the same as those with which he was familiar in the United States. None of the personnel with whom he came in contact exhibited any unusual diseases, except a Negro soldier who had tinea imbricata.

While aboard ship Kley<sup>4</sup> observed that by far the greatest number of visits to the sick bay were for fungous infections, with furuncles incident to acne vulgaris second in frequency of occurrence. The lack of proper bathing facilities, the crowded condition of the crew's quarters and the high atmospheric temperature of the tropics were listed as the factors contributing to the frequency and aggravation of all diseases of the skin aboard ship.

Cohen,<sup>5</sup> who was also stationed at an advance base in the tropics, stated that diseases of the skin are a major cause of disability among military personnel in that area. He noted intolerance to acceptable drugs and to methods of treatment which in temperate climates are

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Material on which this article is based is presented through the cooperation of Captain M D Willcutts (MC), U S N, and Captain James F. Hays (MC), U S N.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

<sup>1</sup> McCarthy, L. Tropical Mycoses, J A M A 123 449 (Oct 23) 1943.

<sup>2</sup> Delaney, J R. Observations of Skin Diseases in the Tropics, U S Nav M Bull 42 1117 (May) 1944.

<sup>3</sup> Ambler, J V. Experience of a Dermatologist in the Southern Pacific, Arch Dermat & Syph 49 224 (March) 1944.

<sup>4</sup> Kley, E C. Skin Diseases Aboard a Destroyer, U S Nav M Bull 42 407 (Feb) 1944.

<sup>5</sup> Cohen, T M. Dermatologic Therapy in the Tropics, U S Nav M Bull 42 1119 (May) 1944.

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employed with impunity. In a review of 1,300 cases which came under his observation in a three month period he found that the incidence of fungous infections was 36.6 per cent. These were most often complicated by a secondary infection or a superimposed dermatitis venenata. Seventy cases of acne vulgaris in severe form also came under observation during this same period. The observations of the men closer to the scene of action and my own are not at particular variance with those of Woolhandler,<sup>6</sup> in an Army station hospital, who found fungous infections to be common and surprisingly extensive. In his series of 3,000 cases, fungous infections headed the list of diseases most commonly encountered. In twenty thousand Army induction examinations, Bereston and Ceccolini<sup>7</sup> found that acne vulgaris headed the list of the twelve most common dermatoses, with fungous infections (not including fungous infections of the feet) number four on the list. The change from civil to military life has in no way influenced the incidence of dermatoses, for in Gilman's<sup>8</sup> survey of the incidence of cutaneous diseases in a student health service, fungous infections head the list, with acne vulgaris second.

In addition to some observations on the treatment of these aggravated forms of fungous infections and indurated and cystic types of acne, this paper will include a discussion of so-called tropical ulcers and a report on 3 cases of exfoliative dermatitis due to quinacrine hydrochloride.

#### PITYRIASIS VERSICOLOR

Clinical variants of pityriasis versicolor have been seen in men evacuated from the South Pacific areas as a brightly erythematous form, which may be circinate or squamous, and as the achromatic form. Heat and humidity undoubtedly account for this variation, and, although it has not been definitely established, the achromia is probably due to the screening action of the scales, similar to the picture seen after desquamation following ultraviolet irradiation of lesions of pityriasis rosea. The eruption involves both the covered and the exposed portions of the skin, with a predilection for the trunk, face and upper extremities.

<sup>6</sup> Woolhandler, H. W. *Dermatology in an Army Station Hospital*, Arch Dermat & Syph **49** 91 (Feb) 1944.

<sup>7</sup> Bereston, E. S., and Ceccolini, E. M. *Incidence of Dermatoses in Twenty Thousand Army Induction Examinations*, Arch Dermat & Syph **47** 844 (June) 1943.

<sup>8</sup> Gilman, R. L. *Incidence of Skin Diseases in a Student Health Service*, Am J M Sc **188** 268 (Aug) 1934.

The treatment of this disease consists in scrubbing the involved areas with tincture of green soap twice daily, followed by the application of an ointment consisting of 1 per cent salicylic acid, and 5 per cent each of precipitated sulfur and juniper tar. In warmer humid climates, to avoid maceration of the skin with an ointment, the application twice daily of 2 per cent iodine crystals in xylene<sup>9</sup> or 2 per cent resorcinol and 5 per cent sulfur in calamine lotion is recommended. Because of the tendency of the eruption to relapse, treatment should be continued for a period of two or three weeks after the clinical signs have disappeared.

#### ERYTHRASMA

Erythrasma is encountered both in tropical and in temperate climates. It involves all intertriginous areas, including the inner side of the thighs and the interdigital webs of the toes as well as the axillary regions, the rectal fold and the umbilicus. The brownish color and the absence of inflammation help to distinguish this disease from pityriasis versicolor, pityriasis rosea and crural ringworm. It may be mistaken for neurodermatitis when thickening of the skin due to scratching supervenes. The treatment is the same as for pityriasis versicolor, except that if lichenification or pustulation is present the treatment must first be directed toward it and then to the parasite.

#### EPIDERMOPHYTON INFECTIONS

In a review of the cases of fungous infections in patients admitted to the hospital, it was seen that the large majority were cases of epidermophyton infections, with involvement of the hands and feet predominating. However, those that have come under my observation differ from the usual case in the frequency with which lymphangitis and regional lymphadenopathy are present. The eruptions vary from the acute vesicopustular and bullous type to the chronic hyperkeratotic type, with varying degrees of resistance to treatment and tendency toward recurrence. Paradoxically, the more severe the infection, with large coalescing blebs and pustules followed by complete exfoliation on the hands and feet, the more rapid is the response to the continuous use of wet compresses with 1:10,000 potassium permanganate solution. This is so consistently true that, in view of recent increased knowledge of the properties of certain fungi, it suggests the production in situ of some

<sup>9</sup> James, A. P. R. *The Fungi Go to War*, U S Nav M Bull **41** 1065 (July) 1943.

yet unknown principle which is toxic to both the fungi and the secondary pyogenic invaders. After the shedding of the superficial epidermis is completed, hastened by débridement, hydrous wool fat, 25 per cent cod liver oil ointment or 10 per cent theobroma oil ointment is sufficient to terminate the case satisfactorily. Excessive sweating, circulatory instability or vascular disease of the extremities, long marches and the necessity of encasing the feet in heavy shoes and prolonged immersion or prolonged wearing of wet shoes and socks are important predisposing factors in fungous disease. Circulatory instability, as evidenced by excessive perspiration and a bluish discoloration of the hands and feet, with maceration of the epidermis, produces a favorable soil for the ingrafting of a fungous infection.

For the subacute variety hot soaks of 1 10,000 potassium permanganate solution for one-half hour twice daily, followed by application of half-strength ointment of benzoic and salicylic acid at night and the application of the following dusting powder after the morning soak, have been efficacious

|                         | Parts |
|-------------------------|-------|
| Salicylic acid          | 1     |
| Menthol                 | 1     |
| Thymol iodide           | 10    |
| Boric acid (pulverized) | 10    |
| Zinc oxide (pulverized) | 10    |
| Talc                    | 10    |

In addition to these procedures, the vesicles and pustules are opened daily before the hands or feet are soaked, the dead epithelium is clipped away, and every three or four days the areas involved are painted with 10 per cent silver nitrate solution followed by the application of 5 per cent solution of merbromin. The latter procedure apparently stimulates keratinization and hastens involution.

The chronic recalcitrant, hyperkeratotic type of epidermophyton infections most often involves the palms, the soles and the lateral surfaces of the hands and feet. For this type, after full strength ointment of benzoic and salicylic acid or 5 per cent chrysarobin ointment fails to bring about the desired results, the following procedure was adopted and can be highly recommended. After the area involved was painted with 10 per cent silver nitrate solution and 5 per cent solution of merbromin or tincture of iodine, it was covered with overlapping strips of adhesive tape. These were left in place from four to six days, after which the hyperkeratotic epidermis was found to be soft and macerated, allowing easy removal. This procedure was re-

peated as often as necessary, and in the event of failure of involution in a reasonable length of time roentgen ray therapy was instituted. Because the field was prepared by preliminary removal of the excessively thickened epidermis, the response was prompt and results were achieved with a fraction of the number of treatments usually required. The same procedure was found equally valuable in the management of localized patches of lichenification and neurodermatitis.

Not infrequently a folliculitis of the distal half of the arm and leg develops, followed by the production of superficial ulcers due to scratching. The lesions responded best to the use of wet dressings combined with the application of 10 per cent silver nitrate solution and 5 per cent solution of merbromin to the denuded areas, or of copper sulfate by iontophoresis. However, the latter type of therapy has not been of value in my experience for any of the other types of involvement.

Tinea cruris, although assuming its usual morphologic characteristics, is occasionally seen associated with a severe inflammatory and exudative type of reaction, which extends to the skin of the entire gluteal cleft. Under treatment with continuous wet dressings of 1 10,000 solution of potassium permanganate, or solution of aluminum acetate, the acuteness of the process readily subsides, and, since relapses are coincident with excessive perspiration, the powder containing thymol iodide but without salicylic acid and with only half the quantity of menthol was of value in keeping the skin dry and forestalling a recurrence after the acute process subsided. When the involvement was limited, a prompt response was obtained by the application of 10 per cent silver nitrate solution and 5 per cent solution of merbromin, followed by sponging two or three times daily with 1 5,000 potassium permanganate solution.

After trial of various medicaments with indifferent results, sodium propionate<sup>10</sup> (10 per cent in talc and 8.2 per cent in normal propyl alcohol in aqueous solution<sup>11</sup>) was found most effective in the treatment of aspergillosis of the ear. The auditory canal was swabbed twice daily with the solution followed by insufflation with the powder.

10 Keeney, E. L., and Broyles, E. N. Sodium Propionate in the Treatment of Superficial Fungous Infections, *Bull. Johns Hopkins Hosp.* 73:479 (Dec) 1943.

11 The sodium propionate solution and powder were supplied by the Mycoloid Laboratories, Inc., Little Falls, N. J.

I have had no personal experience with the group of fungous diseases described as the tropical epidermomycoses and divided by Langeron<sup>12</sup> into four groups, as follows

1 Endodermophytoses, produced by a group of endodermophytions (resembling trichophytions), with a faviform growth on culture, which



Fig 1—Multiple linear scars with rolled-up edges and extension of lesion at border

attack only the skin—never the hair or deeper structures—to form kerion or granulomatous lesions. They do not invade the blood stream. In this group are found *tinea imbricata*, *chumbeire* and *tinea intersecta*.

2 The cladosporian dermatoses (*heimodendron* and *Cladosporium*). Two types are recognized (1) the achromatic type (parasitic achromia of Jeanselme) and (2) the hyperchromic types (*tinea nigra* and *keratomycosis nigricans palmaris*).

3 The dermatoses caused by parasites that produce aleurospores (*tinea albigena*, *kh-hueri*). This type may produce mycetomas as well as involve the skin.

4 Two dermatoses probably due to trichophytions but insufficiently studied (tropical ringworm of Sabouraud and *tinea nigrocircinata*).

As time goes on and men return from the four corners of the earth, even these rare and yet insufficiently studied fungous diseases will demand the best effort and attention of the members of the medical profession.

<sup>12</sup> Langeron, M, cited by McCarthy, in Darier, J, and others. *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, vol 2, p 335.

## CYSTIC ACNE

Many patients with simple acne vulgaris, for which they had not sought treatment while in the United States, were evacuated because the disease had progressed to a degree which disabled them for service. Not only the climate but long hours below deck in the oil-filled atmosphere of the extremely hot engine room is often a factor in causing a mild simple acne to progress to the cystic and infected variety, which is decidedly disabling during warfare over terrain where man must often be his own pack animal. In order to hasten the involution of the lesions and expedite the return of such men to full duty, in keeping with the motto of the medical department of the United States Navy, "to keep as many men at as many guns as many days as possible," this problem was discussed with one of my colleagues, Commander J. P.



Fig 2—"Exteriorized" lesions completely healed, leaving smooth, soft, flat scars.

Nesselrod, who has had considerable experience in the treatment of pilonidal cysts with the method of "exteriorization" described by Buie<sup>13</sup>. Confronted with the deep cystic lesions of acne on the back, chest, neck and face and the unsatis-

<sup>13</sup> Buie, L. A. *Practical Proctology*, Philadelphia, W. B. Saunders Company, 1938, p 480.

factory results of treatment, he felt justified in attempting a careful application of this method to these troublesome lesions

The involved areas were marked by means of methylthionine chloride or gentian violet, and the surface was then cleansed with soap and water. The patient was prepared for operation, and the anesthetic used was pentothal sodium administered intravenously. After a small incision had been made over the cystic lesion, one blade of a long-bladed scissors was inserted into the cyst cavity, thus facilitating an exploration to determine its extent, and the overhanging edges were completely excised. No attempt was made to place marginal sutures. An occasional ligature was found necessary. The wound was lightly packed with iodoform gauze and a dressing held in place temporarily during similar surgical treatment of the remaining lesions. The area was allowed to fill with granulations, and

units. The bacteriologic and laboratory observations, together with the clinical progress in each case are set forth in the table. There were no toxic effects noted in any of the patients.

Further study on the use of penicillin as a topical application in an ointment base, as advocated by Clark,<sup>15</sup> is now in progress.

#### TROPICAL ULCERS

Three patients with tropical ulcers have come under my observation in the past six months, and considering the prevalence of the disease in the Southwest Pacific areas, this small number speaks well for the excellent management of such lesions in the field. All the patients had had malaria, which may be listed as a contributory factor in their debilitated state.<sup>16</sup> In each the lesion was located on the lower part of the leg and occurred after an insect bite which was subsequently traumatized by scratching. One pa-

*Laboratory Observations and Clinical Progress of Patients Treated with Penicillin*

| Patient Number | Clinical Observations  | Culture  | Total Dose of Penicillin, Units | Days Treated, Number | Local Treatment  | Results  |
|----------------|--|--|---------------------------------|----------------------|--|--|
| 1              | Deep seated abscesses of neck, back, chest, shoulders  | Staph aureus                                     | 960,000,000*                    | 8                    | Hot packs, wet dressings of isotonic solution of sodium chloride | Decreased drainage, fourth day, controlled, seventh day                  |
| 2              | Numerous cystic nodules of face, neck, chest, back, many draining thick purulent material. Considerable hypertrophic scarring of old lesions | Staph aureus and Staph albus                     | 2,055,000,000                   | 18                   | Potassium permanganate (1:10,000) locally                        | Improved, fourth day, recurred one week after treatment was discontinued |
| 3              | Draining abscesses of face, chest, back, buttocks  | Hemolytic Staph aureus, nonhemolytic Staph albus | 490,000,000                     | 6                    | None   | Greatly decreased drainage, end of 48 hours                              |

in due time healing took place, with the formation of a small smooth scar over which the patient could shave without discomfort. Six patients have now been treated, with gratifying results, obviating the dimpled and puckered scars with rolled-up edges, that are both unsightly and hazardous from the standpoint of shaving.

Because bacteriologic study revealed the presence of organisms susceptible to penicillin,<sup>14</sup> patients with widespread involvement, in whose health records were noted many admissions to hospitals because of their disability and of the rather indifferent results with all accepted methods of treatment, were treated with penicillin. Three patients have been treated with penicillin to date, and, although the results were anticipated, they were, nevertheless, remarkable. In every instance the drug was administered intramuscularly every three hours in doses of 10,000

units. The patient attributed the rapid spread of the lesion to the fact that ants fed on the serous exudate, and undoubtedly they further contaminated the area. Cohen<sup>5</sup> obtained complete healing in from eight to twenty days with the application of hot compresses of potassium permanganate solution applied for twenty minutes three times daily, followed by 5 per cent sulfathiazole ointment. My routine has been to render the ulcer bacteriologically clean, as advocated by Dostrovsky and Sagher,<sup>17</sup> with the liberal application of a finely milled powder, consisting of equal parts of sulfathiazole and sulfadiazine, and application of a dressing of isotonic solution of sodium chloride. Bacteriologic investigation in my cases revealed the presence of a mixed infection of

14 Hobby, G. L., Meyer, K., and Chaffee, E. Activity of Penicillin in Vitro, *Proc Soc Exper Biol & Med* 50:277 (June) 1942. Dawson, M. H., and others. Penicillin as a Chemotherapeutic Agent, *Ann Int Med* 19:707 (Nov) 1943.

15 Clark, A. M., and others. Penicillin and Procamidine in Burns. Elimination of Haemolytic Streptococci and Staphylococci, *Lancet* 1:605 (May 15) 1943.

16 Costa, O. G. Severe Tropical Ulcer, *Arch Dermat & Syph* 48:414 (Oct) 1943.

17 Dostrovsky, A., and Sagher, F. Phagedenic Ulcer (Pyoderma Gangraenosum), *Arch Dermat & Syph* 48:164 (Aug) 1943.

*Staphylococcus aureus* and *Staphylococcus albus*, beta hemolytic streptococci and a diphtheroid bacillus

As soon as the ulcer was clean and the base covered with healthy granulation tissue, the moist chamber treatment devised by Bier,<sup>18</sup> was instituted. An Ace bandage was applied and the patient was permitted to be ambulatory. A modification of this procedure in treating deep ulcers consists in filling the cavity with dry plasma; this method has been found to be of real value in hastening healing and returning the patient to duty. The rationale has not been investigated but from the standpoint of furnishing proliferating cells with an abundance of a normal num-



Fig 3—Ulcers on the lower part of the shin, which developed after scratching an insect bite. The ulcer has been decreased almost 50 per cent from its original size under treatment.

trient medium in concentrated form it can hardly be improved on. The simplicity of this treatment, coupled with the fact that the patient can be ambulatory for the greater part of the period of hospitalization, recommends it.

#### EXFOLIATIVE DERMATITIS DUE TO QUINACRINE HYDROCHLORIDE

Urticaria<sup>19</sup> and toxic exanthems<sup>20</sup> have been previously reported in patients undergoing therapy with quinacrine hydrochloride. However, a more serious generalized exfoliative erythro-

18 Bier, A. Regeneration und Narbenbildung in offenen Wunden, die Gewebslücken aufweisen, *Berlin Wehnschr* 54 201, 1917.

19 Nayudu, R. V. N. Malaria and Its Treatment by Synthetic Remedies Atabrin and Plasmochin, *Indian M Gaz* 72 531 (Sept) 1937.

derma following quinacrine therapy was first reported by Noojin and Callaway.<sup>21</sup> It occurred in a white woman, aged 45, who, because of chills and fever, took a course of quinacrine hydrochloride, consisting of 0.1 Gm three times daily for five days. Three weeks later the blood smear was positive for plasmodia, and she was given a second course of quinacrine hydrochloride in the same dosage for six days. Several days after the second course she complained of generalized pruritus with a feeling of thickening and soreness of her entire skin. Shortly thereafter a generalized edema with redness, oozing and exfoliation developed, with extensive superimposed infection due to scratching. The white blood cell count rose to 18,650, with 60 per cent eosinophils, and the patch test, with quinacrine hydrochloride elicited a positive reaction. Although lessened in intensity, a reaction was positive even after four months.

#### REPORT OF CASES

CASE 1—S. W., BM 2/c, U.S.N., aged 43, was admitted to the hospital on May 17, 1943, as an evacuee from Guadalcanal, with a diagnosis of exfoliative dermatitis. He had been receiving suppressive quinacrine hydrochloride therapy for almost three months when, in February, he noticed swelling and redness of the feet and legs, with rapid extension to involve the entire body. This was associated with considerable serous oozing and crusting, at one time necessitating dressings over the complete body. After two transfusions, on April 8 and 10, the erythema and edema subsided, leaving the skin a dirty grayish brown. Subjective symptoms consisted of itching and burning.

The patient was admitted to the hospital on May 17, 1943, and the dermatologic examination revealed generalized grayish brown hyperpigmentation and a generalized pea-sized to olive-sized enlargement of lymph nodes. The nails had recently been shed, and the hair was sparse and lacked the normal luster. The spleen was not palpable. There was generalized brawny desquamation and lighter reticulation where the pigmented skin had been denuded after scratching and invasion by secondary infections. Both legs revealed a pitting edema, extending almost to the knees. The leukocytes ranged up to 18,000, with eosinophils to 7 per cent. The differential count was otherwise within normal limits, and there was moderate secondary anemia. The icterus index was normal, and a smear was negative for malarial parasites. A patch test to quinacrine hydrochloride elicited a papulovesicular reaction in twenty-four hours.

Under general supportive treatment the patient made favorable progress up to May 26, 1943, when a basal pneumonia was ushered in by a chill and a rise in

20 Storey, W. E. Toxic Exanthema Following Prolonged Atabrine Administration and Resembling Brill's Typhus Fever. Report of Case, *J. M. A. Georgia* 27 317 (Aug) 1938.

21 Noojin, R. O., and Callaway, J. L. Generalized Exfoliative Erythroderma Following Atabrine. Report of a Case, *North Carolina M J* 3 239 (May) 1942.

temperature to 102.6 F. Coincident with this, the skin became edematous and erythematous, and by June 20, 1943, he again had complete exfoliation. After this second exfoliation the skin was appreciably lighter, but edema, erythema and scaling, together with serous exudation of the legs, persisted for some months. His general health remained good up to Oct 13, 1943, when a third period of generalized exfoliation was ushered in with a temperature of 104 F. At the end of two weeks his skin was again dry and scaly and was a few shades lighter than it was previous to the desquamation. His progress was satisfactory from then until he left the hospital.

CASE 2—E. A. W., a Marine private aged 23, was admitted to the hospital on May 30, 1943, with a diagnosis of exfoliative dermatitis, which first appeared in March 1943 on the chest and arms, after six weeks of suppressive therapy with quinacrine hydrochloride. After an intervening attack of malaria, the eruption became generalized. When the patient was admitted to the hospital, examination revealed an undernourished man with a generalized brownish pigmentation and scaling of the skin, thinning of the hair and shedding of the nails, with thickening and oozing in the flexures of the arms and around the neck. There was a generalized pea-sized to olive-sized enlargement of

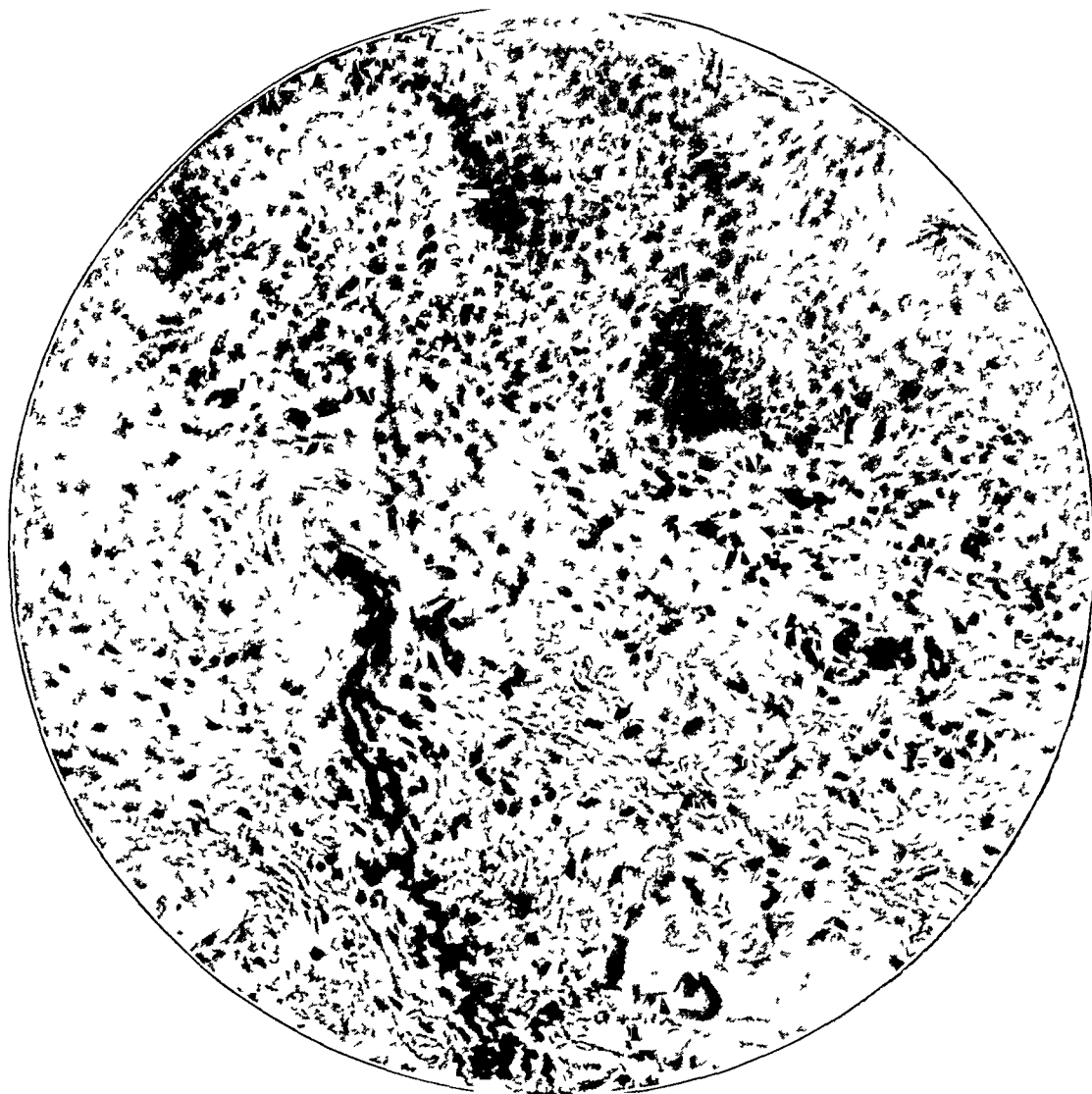


Fig 4—Section of skin showing numerous histiocytes filled with pigment granules in the upper part of the corium.

*Histologic Observations*—A section of skin and a lymph node from the right inguinal region, measuring 3.5 by 1.8 by 1 cm, were removed for study. The epidermis was somewhat atrophic, and the rete pegs were flattened. In the upper part of the corium there was an infiltrate of lymphocytes and plasma cells. Scattered throughout this area there were numerous histiocytes filled with yellowish brown pigment granules.

The lymph node was hyperplastic, with pronounced reticular hyperplasia. The lymphocytes were normal in appearance, but scattered irregularly throughout the node there were large cells filled with yellow pigment granules. Collections of plasma cells were numerous throughout the section, and the architecture of the node was somewhat disorganized, but normal follicles were present. Klemperer and Davidsohn<sup>22</sup> have designated this picture as dermatopathic lymphadenopathy.

lymph nodes. The axillae and groins had the velvety pigmented appearance characteristic of acanthosis nigricans. No plasmodia were noted in the blood smear. The white blood cells ranged up to 13,400, with the eosinophils up to 45 per cent. The patch test with quinacrine hydrochloride elicited a positive reaction.

With colloidal baths, cleansing the skin with cottonseed oil and the application of a 10 per cent theobroma oil ointment, the acute phase of the eruption gradually subsided and the hyperpigmentation faded. Two months after his entrance into the hospital he had gained 30 pounds (13.6 Kg) and was permitted to return to his

<sup>22</sup> Klemperer, P., and Davidsohn, I. Paper read at the Tumor Seminar of the American Society of Clinical Pathologists, Philadelphia, June 2, 1942.

home for convalescent leave. Subsequently he had a relapse of malaria and was inadvertently given quinacrine hydrochloride, which provoked a recurrence of the eruption.

CASE 3—V Z DeJ, an ensign aged 32, was first admitted to the sick list on March 3, 1944, with a diagnosis of contact dermatitis because of an eruption on the neck, arms and legs of three months' duration. He had been given suppressive quinacrine hydrochloride therapy since about Aug 1, 1943, and had taken no other medicament. The eruption was erythematopapular and became generalized on April 9, 1944, when the diagnosis was changed to exfoliative dermatitis

and the spleen was not palpable. The hair was sparse, several toe nails were absent, and all remaining nails showed transverse striation and were frayed at the free edge. Examination of the blood revealed 5,200,000 red blood cells and 14,500 white blood cells, with a normal differential count. The blood smear was negative for malarial parasites.

A patch test with a saturated solution of quinacrine hydrochloride was applied to the left forearm, and at the end of forty-eight hours a papuloerythematous reaction was noted. At the end of seventy-two hours it became vesicular, and on the fifth day the vesicles had dried.

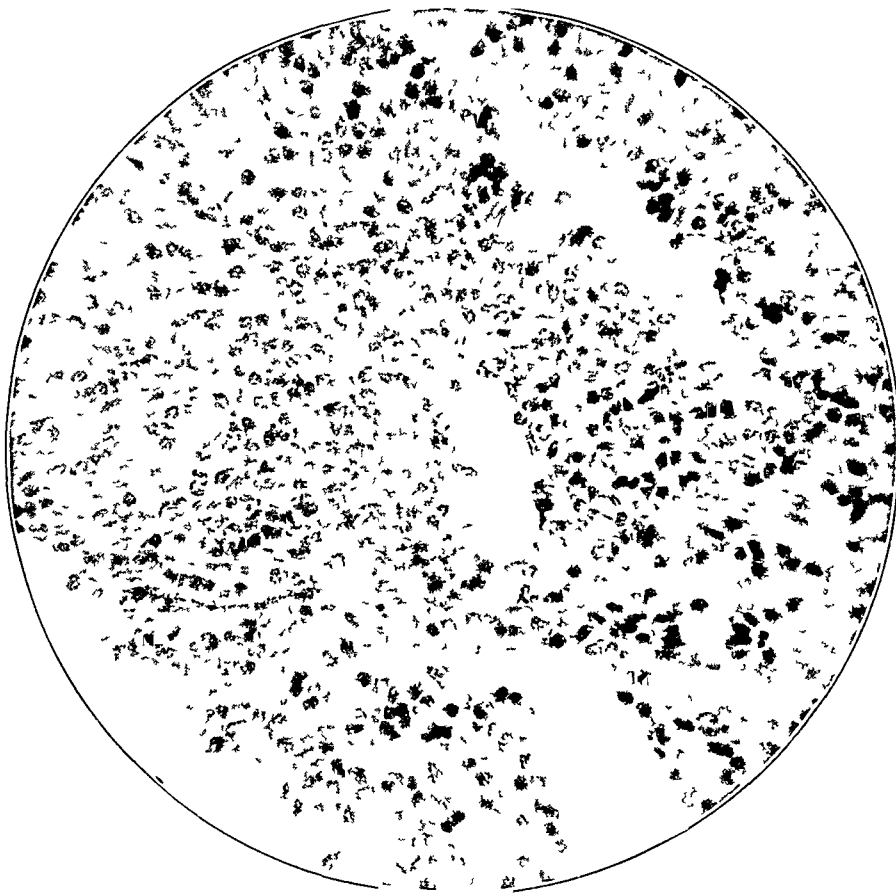


Fig 5—Section of inguinal node showing large cells filled with pigment granules scattered irregularly throughout.

The examination at this time revealed generalized scaling, crusting, fissuring and weeping, and motion was painful because of the heavy crusting in the flexures and the leathery texture of the skin. The temperature was 101 F. The liver was palpable 3 fingerbreadths below the costal margin. The spleen was not palpable. There was a generalized lymphadenopathy, with the largest and most tender nodes in the inguinal region. Both legs and ankles were edematous and pitted on pressure. Under symptomatic and supportive treatment the severity of these manifestations subsided, and the patient returned to continental United States.

He came under my observation on May 28, 1944, presenting a papulosquamous eruption of the legs, neck and arms, with residual grayish hyperpigmentation most pronounced in the axillas and groins. The lymphadenopathy had subsided somewhat, but the axillary and inguinal lymph nodes were still easily palpable and averaged about 1.5 cm in diameter. The liver was palpable about 1 fingerbreadth below the costal margin,

#### COMMENT

A high incidence of disability due to diseases of the skin exists among the armed forces, whether afloat or ashore, in the Southwest Pacific or in more temperate climates. The unfavorable conditions of heat, humidity and filth ashore, the lack of proper bathing facilities and the crowded condition of the crew's quarters, together with long hours below deck in the oil-filled atmosphere of the extremely hot engine room, are significant factors contributing to this high incidence and accounting for complications which make men unfit for duty. Under such conditions it is little wonder that "the fungi go to war," and that the most common lesion is that of a fungous infection, usually complicated



by secondary infection, cellulitis, lymphangitis or lymphadenopathy. Paradoxically, the more severe the infection the more rapid is the response to treatment based on the severity of the dermatitis rather than on the specificity of the offending invader. This happens with such regularity that, in view of recent newer knowledge of the properties of certain fungi, it suggests the production in situ of some yet unknown principle, which is toxic both to the fungus and to secondary pyogenic invaders. The application of silver nitrate solution followed by solution of merbromin has been a valuable procedure in stimulating keratinization, and closure of chronic hyperkeratotic areas on the soles with overlapping strips of adhesive tape has hastened the involution of this recalcitrant type of infection.

The factors operative in fungous infections are also the basis for many cases of mild acne vulgaris progressing to a service-disabling degree. Simple incision and drainage have been found inadequate in the management of such lesions, and a method of "exteriorization" is suggested as a means of terminating this disability and producing a cosmetically acceptable end result. When the involvement is widespread, penicillin produces remarkable results, but exacerbations can be looked for unless the treatment is continued until every focus of infection has been eradicated.

The so-called tropical ulcers are traumatic in origin, and their rapid extension is due to poor personal hygiene and poor facilities for proper care at the time of the injury. When the crater of the ulcers is deep, a modification of the moist chamber treatment, consisting of filling the crater with dried plasma, has been found to hasten filling of the defect and closure of the ulcer.

That quinacrine hydrochloride is capable of sensitizing the skin is shown in the 3 cases of exfoliative dermatitis recorded here. After the acute phase of the eruption passes, a grayish brown pigmentation with retiform depigmentation due to fissuring and superficial denudation of the epidermis remains, which persists for many months but becomes less intense with successive exfoliations. The histologic changes are compatible with those described in dermatopathic lymphadenopathy and are characterized by the presence of histiocytes in the upper portion of the corium and in the lymph nodes filled with yellowish brown pigment granules.

#### ABSTRACT OF DISCUSSION

COMMANDER ROBERT L. GILMAN, (MC), USNR  
I do not know of any one who has had a larger experience in dermatology in the Navy than Lieutenant Commander Duemling, possibly because of his location,

and I am sure that he has had more patients under his care in his department than any of the rest of us have had. He is the dermatologic spokesman for those of us who are treating dermatologic patients in the Navy.

The fact that most of his patients came from the South and Southwest Pacific does not detract from the fact that the ratio of incidence of disease is practically the same, no matter from what area patients come—whether they come from the Atlantic, the tropics or the seaboard.

It is interesting to know that the ratio of cases and the types of cases, are the same as in civilian life, with a few modifications. Medical officers who are practicing dermatology in the armed forces had the same sort of situation to put up with that you do—that is, with overtreatment—plus the fact, as has been pointed out, that certain patients coming from the tropics with diseases of the skin have an unusual susceptibility to ordinary mild medicaments.

The overtreatment of patients is due largely to the fact that some corpsmen at isolated posts use everything they know of—strong potassium permanganate solutions, iodine and ammoniated mercury.

I do not think that one needs to qualify the term "tropical ulcer" with the word "so-called" any more. It is generally conceded that all ulcers contracted in the South Pacific are tropical indeed. The ones I have seen have been traumatic in origin. There is no one on shipboard who has not banged his shin from time to time, and the resulting ulcer may or may not heal promptly. If it opens and has to be treated, the man must be put in sickbay for a long period, and rest in bed is one of the most important aspects of therapy.

I have not observed the number of cases of acne that Lieutenant Commander Duemling has encountered. But those who subscribe to the theory that carbohydrates influence or cause acne need not be reminded that the average sailor lives on candy bars, ice cream and carbonated drinks. There may be something in that fact in addition to the effect of oil and a humid atmosphere on cutaneous diseases.

When I first went into the service, I expected to see a wide variety of unique and unusual tropical cutaneous diseases, but I soon found out that tropical dermatoses are the same as those seen in civilian life excepting that they are a little harder to handle.

The first observation I made of this fact was in the Caribbean. I can tell about it now. Maybe I am naive, but I had not seen before the type of scabies that I saw there. There are few cases of the textbook or classic types of scabies, but I did see a number of patients with scabies whose lesions were confined solely to the penis, and the diagnosis had to be made from that evidence alone. These patients had no lesions on the webs of the fingers or the wrists or in the axillae. I thought that this observation was particularly important because previously some of these patients had been examined and were treated for multiple chancroid and in some instances for multiple chancres.

Another disease which I have found most refractive and disabling is prickly heat. One is less apt to see it in this country at shore establishments. One sees it at sea, where there is often a large drain on water, but more frequently it occurs in the regions just above and just below the Equator. It is exasperating and readily lends itself to secondary infection.

My most recent experience associated with the practice of medicine in the Navy has been to encounter,



during the last two or three weeks, multiple epitheliomas in groups of eight or ten occurring in men, usually blond, ranging from 30 to 38 years old

DR JAMES H MITCHELL, Chicago The remarks of Dr Paido-Castello concerning the limitation of the lesions of scabies to the penis in Cuba, and the frequency of the lesions on the male genitalia in other countries suggest that the explanation of this phenomenon may be that there is an absence of Lesbians among the female acarids

I have never been able to decide whether Dr Ormsby and I did more harm than good when our paper on ringworm of the hands and feet was presented at Detroit, in 1916 The widespread tendency since that time to treat all acrodermatoses as ringworm, without an effort to establish a diagnosis by microscopic examination, has resulted in untold discomfort, not to say suffering, on the part of many patients

Looking at the pictures shown by Lieutenant Commander Duemling inclines me to the belief that many of the cases are of mixed pyogenic infections rather than of fungous infections, and I am pleased that Lieutenant Commander Duemling is of the same opinion He has changed his treatment with this in mind, and his results justify the change

I should like to ask how many of these cases were controlled microscopically and culturally My recent experience as examiner in mycology on the American Board of Dermatology and Syphilology was illuminating Only one of the forty candidates recognized a fresh preparation containing many organisms of *Pityrosporum furfur*, and it should be known that this candidate was a woman Fungi were overlooked when they were left in focus in the field and found in preparations in which none were present Fuseaux were pointed out beside a hair, spores were overlooked in infected hairs and found in normal hairs

I should also like to ask whether lichen-planus-like lesions have been seen in men taking quinacrine hydrochloride Dr Caro and I have presented some patients in whom there were found lesions which closely simulated lichen planus clinically and histologically

I believe that it will be found eventually that there is a lichen-planus-like eruption produced by quinacrine hydrochloride, and I would suggest that the dermatologists be on the watch for it

DR SAMUEL AYRES JR, Los Angeles I am happy to have had Lieutenant Commander Duemling clarify the situation regarding tropical ulcers and desert sores, because it seems to be a matter of considerable confusion in recent literature Cases that are reported from the Pacific area seem to be described as cases of tropical ulcers, and those that come from North Africa as cases of "desert sore," and some authors attempt to differentiate between them Hence I think that it has been constructive to have this expression of opinion

One other point with regard to the question of the deep cystic acne Lieutenant Commander Duemling mentioned 1 case in which relapse occurred immediately after treatment with penicillin I am wondering whether any of the patients so treated remained cured

It has been my belief that the deep cystic-abscess-like burrowing lesion represents a sensitivity of the tissues as much to the organism as to the virulence of the organism itself Desensitization of the tissues by means of intravenously administered autogenous vaccines, according to the method that was described originally by Clausen and Allen in the treatment of arthritis, I have found to give good results—in con-

junction, of course, with other measures—with a fair prospect that they will be lasting

The mention of the infection following flash burns calls to mind a recent contribution by Lieutenant Commander Pendleton, of the Mare Island Naval Hospital, in which he advocated the use of a mixture of paraffin with a suspension of sulfanilamide and other ingredients to be sprayed on with an ordinary insect spray gun in the treatment of burns of all types

During the time when bombings were expected, I began to wonder just how I as a dermatologist might be of use in the emergency It seemed that handling burns would be a little more logical than treatment, for instance, of chest injuries I made it my business to investigate the latest developments in treatment of burns

I have had a rather limited experience with the use of the Pendleton technic in 1 case of a severe burn, and it is certainly a most satisfactory method

Dr Anderson and I used this technic in treating a patient with a flash burn on the face from gasoline, and the results were gratifying

The prompt use of the paraffin spray, which is entirely different from the paraffin method used during the last war and requires no dressings whatsoever as it makes a thin pliable film, has many advantages The presence of a small amount of sulfanilamide in suspension inhibits infection, and it seems to be a technic well worthy of further use Pain is relieved, scarring minimized and free movement of the affected area permitted

DR C GUY LANE, Boston I believe that we owe a great deal to Lieutenant Commander Duemling for his presentation today from another aspect I think that teachers here at home depend on medical officers come back from the various services to describe their problems and tell what is happening in the theaters of war In the instruction of senior students I feel that the teacher can emphasize those problems which the physicians in service have described, because before long the students go into military service and handle just such cases

I think that Lieutenant Commander Duemling has emphasized well the types of disease which he and his colleagues are seeing He has also emphasized well the need for us to warn our students about the matter of drastic therapy

He speaks of overtreatment by corpsmen and others The teacher can emphasize to his students the fact that overtreatment is a problem and that they should be extremely careful with regard to the treatment of acute phases of any disease

DR EVERETT S LAIN, Oklahoma City Lieutenant Commander Duemling has given a most interesting and important review of a practical subject

In the discussion of this subject, Dr Gilman has brought up a question about which we are to hear more tomorrow, namely, the possible effect of solar radiation on malignant growths of the epithelium Recently the report has come to me of the high incidence of cutaneous malignant growths occurring in the boys who have been retained in the South Pacific area one or more years Because of illness I have personally seen only a few returning soldiers Already I have seen 2 cases of cancer of the skin in medical officers who had been in the South Pacific two years or longer

After hearing Lieutenant Commander Duemling's report on the use of penicillin for pustular acne, I was reminded to report a case of severe dermatitis herpetiformis in which I used penicillin The patient is a veteran of World War I, with dermatitis herpetiformis

which has gradually grown worse from year to year. My diagnosis has been confirmed by several of the dermatologists here today, who have seen this patient presented at various clinics.

Eventually, I obtained permission to use penicillin in this case. I was encouraged to use penicillin because the patient takes sulfathiazole almost by the handfuls. He deliberately pours out 10 or 12 or 15 tablets at one time and swallows them and tolerates them perfectly. This almost clears the eruption within forty-eight to seventy-two hours. Of course, his blood count is guarded, and he does not take such a dose oftener than once a month.

Recently, I have given this veteran 900,000 units of penicillin. He began to improve within twenty-four hours. He was approximately clear of all new lesions in five days. He has now been clear for a period of only three weeks. Therefore, I do not know whether the improvement will be permanent. I report the case only that others may be encouraged to try penicillin in like cases of dermatitis herpetiformis.

DR HOWARD FOX, New York. For years there has been a good deal of dispute, or at least misunderstanding, about the term "tropical ulcer."

Lieutenant Commander Duemling speaks of the tropical ulcers which he saw as being due to traumatism. The textbooks on tropical medicine say that tropical ulcer is a definite entity due to Vincent's organisms. As Dr Ayres said, there is a great deal of confusion between desert sore and tropical ulcer. Some physicians use the term "tropical ulcer" for all kinds of ulcers that occur in the tropics.

I should like to ask Lieutenant Commander Duemling whether he examined any of his patients for Vincent's organisms.

DR JOHN G. DOWNING, Boston. I should like to ask Lieutenant Commander Duemling one question. Were any control tests for quinacrine hydrochloride made on normal persons?

DR GEORGE M. LEWIS, New York. There is still a considerable lack of understanding and indifference among the undergraduate medical students as to the seriousness of this and related problems.

When one takes the figures given in Lieutenant Commander Duemling's interesting paper, it is seen that 1 per cent of all the disabilities in the armed forces are due to fungous disease. There is also a considerable number of cases in which the disease is not serious enough to warrant disability.

In a communication in *The Journal of the American Medical Association* (123:449 [Oct 23] 1943) McCarthy gave a picture similar to that which we have now had from Lieutenant Commander Duemling. This confirms the statement that most of the dermatoses seen in members of the armed forces are of the ordinary variety of fungous diseases, with accentuation on the severity of symptoms due to service conditions.

I should like to agree with and emphasize Dr Mitchell's discussion. It would seem important that in each case there should be determination of the organism by culture, if for no other reason than that not all the fungous diseases acquired in the far corners of the world will be of the ordinary types. I feel that some unusual diseases may be expected, and the dermatologists in the armed forces will have the first opportunity to study them.

One specimen was sent to me by Lieut Comdr Robert Lofgren from the Central Pacific area. It was of interest that I was able to grow *Microsporon ferrugineum* on this culture; this is a very unusual fungus

in the United States although a fairly common one in the Orient. One may encounter cases of fungous disease due to this micro-organism among troops returning from this theater of war.

The question of prevention is important. I hope that Lieutenant Commander Duemling in closing will tell how he attempts prophylaxis. I know that Dr Howard Fox believes in the usefulness of plain talc, to which I subscribe. In my experience plain powder (purified talc USP), either fortified or not with fungicides, is an effective prophylactic agent.

DR SAMUEL M. PECK, Bethesda, Md. The question of the prophylaxis of fungous infections of the feet has been taken up in great detail by Dr Hopkins' committee of the National Research Council.

I am convinced that a medicated foot powder is much more efficacious than talc alone. More and more of the workers in the field of fungous infections have come to the conclusion that foot baths are not efficacious as a control measure against dermatophytoses. This is especially interesting in view of a recent study which my associates and I made (*Dermatophytoses in Industry*, ARCH DERMAT & SYPH 5:170 [Sept] 1944), which seems to indicate that shower room flooring plays a minor role in the spread of fungous infections of the feet.

DR CLINTON W. LANE, St. Louis. I should like to ask if ointments containing sulfonamide compounds are being used as widely and indiscriminately by the medical officers in the armed forces as by physicians in private practice and if proprietary sulfonamide ointments are issued to corpsmen for use without the supervision of a physician.

DR FRED D. WEIDMAN, Philadelphia. May I ask whether aspergillosis of the ear has received attention, although it is on the borderline between the specialties of otology and of dermatology. I understand that this disease is a veritable scourge in the Canal Zone and in other places in the tropics.

The otologists seem to have decided on cresatin-Sulzberger (metacresylacetate) as the best agent in treating this disease. On the strength of that, Dr Frederic Glass and I conducted a survey of conditions of the feet of inmates in a penitentiary. We did not call it a study of dermatophytosis, because we did not want to narrow our considerations to fungous infections. On a group of 100 convicts, over whom there was nearly perfect control, we conducted comparative tests using cresatin-Sulzberger, boric acid foot powder (10 per cent in powdered talc), ointment of benzoic and salicylic acid and three proprietary preparations, namely, zephiran and pomeio (potassium mercuric iodide) and Iodolate (iodocholate). We found that cresatin-Sulzberger and boric acid powder were about equal in effectiveness. Incidentally, these tests were conducted in the wintertime, and none of the lesions were severe eczematoid ones. It appears that if a really active fungicide is to be employed, cresatin-Sulzberger should be included.

Although not all of Australia is in the tropics, it has a significance in tropical war areas. It should be remembered that one particular form of favus, namely mouse favus, is endemic there. This situation is due to the wheat "industry." Mice make their nests in the sacks, and in handling the sacks the men contract the disease.

DR V. PARDO-CASTELLO, Habana, Cuba. I should like to make a few remarks about the paper by Lieutenant Commander Duemling, since I grew up among all these diseases in the Caribbean tropics. I can vouch

for the fact that the diseases that Lieutenant Commander Duemling has described from the Pacific tropics are exactly the same as occur in the Caribbean tropics.

I want to say, particularly, that I was pleased about the interpretation of the condition called "tropical ulcer." I do not believe that there is one entity that can be called "tropical ulcer." I think that tropical ulcers are infected lesions resulting from trauma and mosquito bites and perhaps, as Dr Fox has remarked, secondary infection of these lesions by Vincent's organisms.

I want to remark also on scabies of the penis. In the Caribbean area, too, one observes many patients with scabies who have only one or two lesions on the penis. Though, of course, the patient complains of generalized itching, there are no typical lesions of scabies elsewhere—only one or two small lesions on the penis.

I recall a case I encountered, in one of the New York hospitals, in Dr Fox's service. The patient had one small ulceration on the dorsum of the penis which would not heal. I suggested that it might be scabies. Of course, members of the staff were much surprised, because they had not considered such a possibility.

The patient was asked whether there was any itching. He said that he had experienced itching at night, but there was no other lesion than that small ulcer on the dorsum of the penis.

As I was sitting here listening to this discussion, I remembered that in another discussion of a similar kind many years ago I remarked before this Association about the absence of ringworm infection of the feet of persons who go barefoot. I want to mention that fact again.

Perhaps Lieutenant Commander Duemling and the other members of the Association who have been in the tropics have made the same observation. For instance, sailors on the coast or serving at the clubs go barefoot all the time. Their feet are always wet, and yet one does not see a case of ringworm of the foot among them. The same thing applies to the newsboys, who go barefoot. With the dirt and the mud and the wetness of the summer showers, one never sees the chronic type of ringworm of the foot. Although they might have pyoderma and secondary infections and lymphangitis, as Lieutenant Commander Duemling has described, one does not see the macerated form or the vesicular form of ringworm among these people.

LIEUT. COMDR W. W. DUEMLING, San Diego. I am indeed grateful for your cordial and helpful discussion. It has been a real privilege for me to meet with you and renew old friendships after two years in the Naval Medical Service.

The point that Dr Gilman mentioned about diet as a factor in acne vulgaris cannot be overlooked in the case of the Navy. I have personally seen them leave the mess where they are well fed, and immediately proceed to Ship's Service, where they gorge themselves on pie and chocolate bars.

Heat rash, which has been a common problem in the South Pacific, has not come to medical attention in the ideal climate of southern California because the rash has disappeared by the time the patient reaches the hospital.

Dr Mitchell's remarks regarding treatment and over-treatment are timely, and I am convinced that better results are obtained when treatment is based on the acuity of the process rather than on the etiologic agent. I am constantly amazed at the splendid job the corpsmen are doing, and, with the recognition that their training is limited but intensive, every effort is made to impress on them the principle that mild and simple medication should be preparations of their first choice. If they adhere to this dictum, one can be assured that they will not go too far astray.

At the present time there is no mycologist on the laboratory staff, hence the fungous infections have not been thoroughly investigated culturally.

Dr Mitchell's observation of a lichen planus type of eruption in patients taking quinacrine hydrochloride is of interest, but to date such an eruption has not come to my attention. The cases reported here cannot be considered as of serious consequence when one balances them against the thousands in which the patient is kept on the job because of suppressive therapy with quinacrine hydrochloride.

Relative to Dr Ayres's remarks about relapse of cystic acne, supplementary treatment was necessary in all cases, but the use of penicillin as a preliminary measure greatly reduced the number of sick days, and the response to treatment was miraculous. However, treatment must be continued until every focus is eradicated.

The best method for the treatment of burns, whether open or closed, has apparently not yet been settled. A committee on the treatment of burns at the Naval Hospital in San Diego subscribes to the use of dressings of hypertonic solution of sodium chloride and the generous use of plasma and morphine to combat shock.

For small flash burns the closed method of treatment offers definite advantages. But this question is still a matter of debate and perhaps will be settled within the coming year. The recent exhibit of Capt Ernest W. Brown, of the Bureau of Medicine and Surgery, on the "Prevention of Burns in the Navy" with the use of a protective ointment and certain clothing offers the best answer to this problem.

I heartily agree with Dr Lane that teachers must constantly lay emphasis on avoidance of overtreatment, because the management of a severe superimposed dermatitis venenata means a wasteful loss of man days and often a prolonged period of hospitalization.

Recent published reports seem to be in agreement with my observation that tropical ulcers are not dependent on any one organism, but the ulcers are usually contaminated with various organisms.

In the Navy no attempt is made at mass preventive measures to control fungous infections, but reliance is placed largely on personal prophylaxis.

Aspergillosis of the ear has been an important cause of disability in personnel on duty in tropical areas. I have read the reports of various activities and the suggestions for the treatment of this troublesome disease. The best results have been predicated on the use of powders (sulfanilamide, sulfathiazole and zinc peroxide) and keeping the ear canal dry.

In my hands the use of sodium propionate (10 per cent in talc and 8.26 per cent in normal propyl alcohol in aqueous solution) has produced good results.

# VINCENT'S DISEASE OF THE SKIN

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This is a report of the case of a patient suffering from Vincent's disease, with lesions affecting the feet, the corners of the mouth the gums, the tongue and the tonsillar and pharyngeal regions. Vincent's infection of the gums in its chronic form is regarded as fairly common. Acute forms affecting the gums and the tonsillar and pharyngeal tissues and even extending to the bronchi and lungs have been recorded. Cutaneous lesions due to fusospirochetal infection have been encountered but in only a comparatively few instances.

An interesting series of cases of acute fusospirochetal angina is that of Goldman and Kully,<sup>1</sup> who reported 7 cases of its occurrence in Negroes with lesions of the buccal and pharyngeal mucous membrane all of which were fatal. Two of the patients had positive serologic reactions, while 3 had cutaneous lesions, ranging from erythematous patches to bullae terminating in shallow ulcers. Direct examination of material from these lesions failed to show the presence of the specific symbiotic organisms. With regard to the positive serologic reactions, the authors stated that in persons with Vincent's disease the Wassermann reaction is negative and is positive only when an associated factor is present. Perry<sup>2</sup> reported 3 instances of Vincent's angina with an erythema multiforme type of eruption. Gilman's<sup>3</sup> patient presented Vincent's infection of the umbilicus associated with pemphigus vulgaris. The condition developed two months after an attack of sore throat. Munkerren<sup>4</sup> described a pemphigoid cutaneous eruption

in a patient with angina. Shulman<sup>5</sup> recorded an instance of Vincent's infection of the nose in a child 3 years old, with a persistent sanguineous mucopurulent discharge and a greenish membranous slough. The disease was associated with Vincent's infection of the gums. There were cervical adenitis and moderate constitutional symptoms.

## REPORT OF A CASE

W. H., a white man aged 23, reported to the clinic of the Skin and Cancer Hospital, complaining that his feet had been painful for the past two months. Walking was difficult, and the feet stung whenever anything touched them. There was a pronounced fetid odor from the feet when the patient removed his stockings. Objec-



Fig 1—Vincent's infection at interspaces of the toes

tively, there were brownish discoloration of the toe nails, evidence of a previous application of potassium permanganate, and swelling of the paronychia tissue, purulent discharge and loosening of the nails from the nail bed. On the left foot between the second and third interspaces there was an ulcer beginning at the base of the affected toes and extending 2 cm toward the free ends of the toes. The ulcer was oval, circumscribed, rather firm and not deep, and the base was covered with pale granulations and seropurulent exudate. The remaining interspaces showed crusting and desquamation. The plantar surfaces were without abnormalities. There was excessive perspiration of both the plantar and the palmar surfaces.

The lips were dry and showed slight fissuring. At the commissures, especially on the left side, there was ulceration, linear in form, with an infiltrated border and with papillary lesions on the cutaneous surface. The fissures extended into the mucous membrane, and the picture closely simulated that of perleche. The gums were swollen, painful and reddened, exudation was

From the Skin Clinic of The Skin and Cancer Hospital

1 Goldman, L., and Kully, H. E. Fatal Fusospirochetal Angina. Report of Seven Cases, *J. A. M. A.* **101** 358 (July 29) 1933.

2 Perry, M. W. Vincent's Angina. *Internat. Clin.* **4** 32 (Dec) 1924.

3 Gilman, R. L. Case of Vincent's Infection of the Umbilicus Associated with Pemphigus, *Arch. Dermat. & Syph.* **25** 556 (March) 1932.

4 Munkerren, E. Durch Spirillen und Bakterien hervorgerufene ulceros-gangranose Entzündung der Mundschleimhaut begleitet von einem Pemphig. *Hautausschlag, Zentralbl. f. Haut- u. Geschlechtskr.* **41** 731, 1932.

5 Shulman, H. I. Vincent's Infection of the Nose, *Am. J. Dis. Child.* **36** 352 (Aug) 1928.

present, and salivation was excessive. The tongue presented fissuring, with areas of denudation irregularly distributed. The tonsillar and the pharyngeal mucosa were reddened and congested.

The patient was a young white man who appeared to be in good health. Aside from an attack of diphtheria in early life, he knew of no illness except the present ailment. Physical examination showed no abnormalities except adenopathy of the cervical, submaxillary and inguinal lymph nodes.

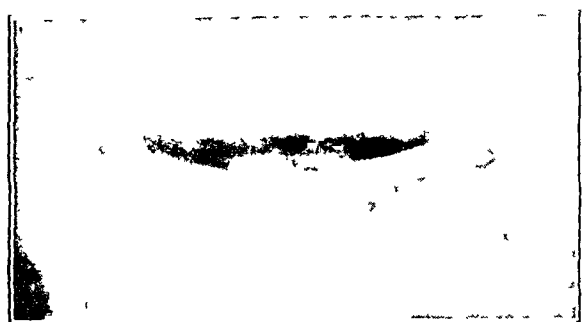


Fig 2—Vincent's infection at commissures of the mouth

*Laboratory Studies*—Direct examination of the various cutaneous lesions for Vincent's organisms was made, with the following results. In the gums were observed a large number of Vincent's spirilla and fusiform bacilli, in the tonsillar and pharyngeal areas, a moderate number of the Vincent symbiotic organisms, in the commissures of the mouth, a moderate number of symbiotic spirilla and bacilli, and in the lesion of the interspaces (ulcer),

a moderate number of Vincent's spirilla and fusiform bacilli. Organisms were not observed in the toe nails and paronychia tissues. An attempt to culture the *Spirillum* was unsuccessful.

The urine was normal. A blood count was normal except for leukocytosis, the sugar and urea nitrogen were within normal limits. The Wassermann and Kahn reactions of the blood were strongly positive (4 +), the spinal fluid reacted negatively to all tests, including the Wassermann and the colloidal gold tests.

*Treatment*—The local treatment consisted of application of sodium perborate to the feet and 10 per cent neoarsphenamine in glycerin to the gums. Thio-bismol in doses of 1 cc was administered intramuscularly twice weekly for four weeks.

The patient remained in the hospital for thirty-six days and was discharged with the feet free of lesions. As the patient disappeared from observation, no additional light can be shed on his positive serologic reactions, and it is most unlikely that the Vincent's infection could have produced the strongly positive Wassermann reaction.

A patient was observed with Vincent's infection of fairly generalized extent. The cutaneous lesions on the feet were associated with a most pronounced fetid odor, a characteristic emphasized by Sutton in his description of this clinical entity. The positive Wassermann reaction of the blood is to be regarded as an incidental observation.

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# LUPUS ERYTHEMATOSUS

## TREATMENT WITH OXOPHENARSINE HYDROCHLORIDE

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Chronic discoid lupus erythematosus has been treated by many methods. It is not the purpose of this paper to review the literature or to describe any or all of these procedures but it is the purpose to submit a report on the results of therapy with biweekly injections of small doses of oxophenarsine hydrochloride (mapharsen).

During the past twenty months, 21 patients with chronic discoid lupus erythematosus have been studied and treated, and the results have been most encouraging. The use of small doses of oxophenarsine hydrochloride in the treatment of this disease was first suggested by Sulzberger<sup>1</sup> and, on several occasions since, its use has been mentioned by Wise<sup>2</sup> in the transactions of dermatologic societies in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. Hyman<sup>3</sup> stated that he used oxophenarsine hydrochloride with excellent results for 16 patients with chronic discoid lupus erythematosus, some of whom had previously been treated unsuccessfully with gold sodium thiosulfate. Baer<sup>4</sup> used oxophenarsine hydrochloride in treating a patient with chronic discoid lupus erythematosus which had disseminated and considered the response better than with any previous therapy.

A chance observation during modified intensive arsenotherapy of a soldier having both syphilis and chronic discoid lupus erythematosus impelled me to use oxophenarsine hydrochloride for the latter disease. The lesions of lupus erythematosus cleared rapidly, and, in order to determine whether this was merely coincidental, more patients were given oxophenarsine hydrochloride.

Twenty-one patients were treated, 19 of them were white persons, and 2 were Negroes. Each

patient, except 1 of the Negroes, had a definite history of sensitivity to light, severe cold, heat or biting wind. Sixty per cent of the patients had had their disease before induction, and the average duration of the dermatosis in 20 cases was about forty-seven months. The remaining patient was an officer who had had the disease for twenty-two years. In all but 3 patients the dermatosis was confined to the scalp, face, nose, ears and neck, the 3 had lesions on their arms and back as well. All but 1 patient were men, and in none were there any constitutional disturbances, such as arthritis, fever, loss of weight or pains in the chest.

Oxophenarsine hydrochloride was given biweekly by vein in doses of 0.02 Gm in 4 cc of distilled water, an amount chosen arbitrarily for its stimulating effect. At no time were there any untoward symptoms. Improvement seemed to take place almost immediately, the patients definitely noticed it after the second injection. The average number of injections given was ten, the range was from 6 to 16. Four patients had increased sedimentation rates, but these returned to normal after treatment was discontinued.

The first objective condition to disappear was the erythema, this was followed by the disappearance of the scaling. The pigmentation was the last to decrease, but it never disappeared entirely, it persisted particularly in the Negro patients. Scarring was not affected, in 1 patient, however, plastic surgical treatment accomplished a remarkable result. It was impossible to determine whether any diminution in sensitivity to light or physical agents occurred, since none of the patients were kept under observation longer than sixty days.

One patient with acute disseminated lupus erythematosus, unaffected by large doses of penicillin, died before oxophenarsine hydrochloride treatment could be instituted.

### SUMMARY AND CONCLUSIONS

Twenty-one patients with chronic discoid lupus erythematosus, 19 of them white persons and

1 Pillsbury, D. M., Sulzberger, M. B., and Livingston, L. S. Manual of Dermatology, Philadelphia, W. B. Saunders Company, 1942, p. 271.

2 Wise, F., in discussion on Klumpp, M. M. Lupus Erythematosus, Arch. Dermat. & Syph. 50: 135 (Aug.) 1944.

3 Hyman, A. B., in discussion on Baer,<sup>4</sup> p. 152.

4 Baer, R. L. Lupus Erythematosus Disseminatus (Treated with Mapharsen), Arch. Dermat. & Syph. 49: 151 (Feb.) 1944.

2 Negroes, were seen in a period of twenty months. All were treated with biweekly injections of 0.02 Gm. of oxophenarsine hydrochloride, with uniformly good results. The average number of injections given was ten, and improvement was usually noted after the second injection. Erythema and scaling were the first signs to disappear. Pigmentation more prominent in the Negro patients, decreased last but did not disappear completely. Scarring was unaffected.

Patients were not observed long enough to determine whether any diminution in sensitivity to a physical agent, such as light, cold, wind or extreme heat, took place. Though this method of treatment has not been attempted for any patients with acute disseminated lupus erythematosus it is hoped that it may be tried in the future.

NOTE.—Since this paper was written, 10 additional patients with chronic discoid lupus erythematosus have been treated by this method with good results.

## ERYTHEMA MULTIFORME

### REPORT OF A CASE OF SEVERE ERYTHEMA MULTIFORME WITH INVOLVEMENT OF THE MUCOUS MEMBRANES TREATED WITH PENICILLIN

H C ROBINSON, M D

GRAND RAPIDS, MICH

Severe erythema multiforme with involvement of the mucous membranes has often gone unrecognized or has been reported under different names. American interest seems to have been renewed by the report of 2 cases in 1922 by Stevens and Johnson<sup>1</sup> of what they believed to be a previously unrecognized clinical entity. Since that time cases of the disease under various names have been reported by Wheeler,<sup>2</sup> Rutherford,<sup>3</sup> Smith,<sup>4</sup> Bailey,<sup>5</sup> Ginandes,<sup>6</sup> Chick and Witzberger,<sup>7</sup> Edgar and Syverton,<sup>8</sup> Ageloff,<sup>9</sup> Levy<sup>10</sup> and Murphy<sup>11</sup>. In 1944 Lever<sup>12</sup> re-

ported 2 cases and thoroughly reviewed the literature. His discussion has tended to clarify the situation, and it is to be hoped that in the future students will recognize the entity, relatively rare and rarely fatal but occasionally leading to loss of vision.

#### REPORT OF CASE

*History*—B T, a schoolboy 15 years old, entered the hospital on the fifth day of definite illness, complaining of a sore mouth.

For a few days prior to the onset of acute illness he was "unduly fatigued and easily upset emotionally." His initial complaint was of a sore throat and mouth, with loss of appetite followed by repeated vomiting. The second day the local physician was called and reported nausea and vomiting. His temperature was 103.6 F, and the pulse rate was 120 per minute. The gums were edematous, and there were plaques on the tongue and posterior pharyngeal wall. The auditory canals were red. Swallowing was difficult. On the third day he was given 1 Gm of sulfadiazine every three hours and a mouth wash of sodium perborate. On the fourth day he seemed apathetic, and the fever and other symptoms persisted. On the fifth day he entered the hospital.

There was a past history of measles, mumps, chickenpox, whooping cough, pneumonia, infantile paralysis and streptococcal infection of the throat. The tonsils had been removed. He had suffered a fracture of the left clavicle and humerus.

The history of the systems was not abnormal.

*Physical Findings and Course*—Physical examination at the time of his entry revealed an acutely ill, drowsy but mentally clear boy, who was well nourished and developed except for partial atrophy of the muscles about the left shoulder, with some limitation of motion. This resulted from the poliomyelitis. The findings were otherwise normal throughout except for enlarged cervical lymph nodes, injected conjunctivas and lesions of the mucous membrane of the mouth.

The lips were dry and cracked and crusted with brownish yellow exudate. There was free salivation. The buccal mucosa, the palate and the dorsal surface of the tongue were injected and covered with glistening creamy white vesicles, varying in diameter from 2 mm to 15 mm. The gums and pharyngeal wall were red and swollen but not covered with the vesicular lesions.

12 Lever, W F. Severe Erythema Multiforme. Report of Two Cases of Type Ectodermosis Erosiva Pluriorificialis, with Development of Cicatricial Conjunctivitis and Keratitis in One Case, *Arch Dermat & Syph* 49 47-56 (Jan) 1944.

1 Stevens, A M, and Johnson, F C. New Eruptive Fever Associated with Stomatitis and Ophthalmia, *Am J Dis Child* 24 526-533 (Dec) 1922.

2 Wheeler, J M. Destructive Purulent Ophthalmia Accompanying an Eruptive Fever with Stomatitis, *Tr Am Acad Ophth* 34 179-190, 1929.

3 Rutherford, C W. Membranous Conjunctivitis with Loss of Eyeballs. Report of Cases, *J A M A* 93 1779-1784 (Dec 7) 1929.

4 Smith, C A. An Unusual Case of Erythema Multiforme, *Tr Univ Michigan Pediat & Infect Dis Soc*, 1929, p 63.

5 Bailey, J H. Lesions of Cornea and Conjunctiva in Erythema Exudativum Multiforme (Heber) Report of Three Cases with Grave Ocular Sequelae, *Arch Ophth* 6 362-379 (Sept) 1931.

6 Ginandes, G J. Eruptive Fever with Stomatitis and Ophthalmia. Atypical Erythema Exudativum Multiforme (Stevens-Johnson), *Am J Dis Child* 49 1148-1160 (May) 1935.

7 Chick, F E, and Witzberger, C M. Erythema Multiforme Exudativum Accompanying Oral Vincent's Infection, *Am J Dis Child* 55 573-578 (March) 1938.

8 Edgar, K J, and Syverton, J T. Erythema Exudativum Multiforme with Ophthalmia and Stomatitis. Report of Two Cases in Children with Certain Observations on Histopathology and Animal Inoculation, *J Pediat* 12 151-159 (Feb) 1938.

9 Ageloff, H. Erythema Multiforme Bullosum with Involvement of Mucous Membranes of Eyes and Mouth (Stevens-Johnson Disease). Report of Case, *New England J Med* 223 217-219 (Aug 8) 1940.

10 Levy, A T. Erythema Multiforme Bullosum with Involvement of Mucous Membranes of Mouth (Stevens-Johnson Disease), *J Am Dent A* 30 287-288 (Feb) 1943.

11 Murphy, R C. Eruptive Fever Involving the Mouth and Eyes (Stevens-Johnson Disease). Report of Case, *New England J Med* 230 69-71 (Jan 20) 1944.



The temperature was 105.4 F, the pulse rate, 105, and the respiratory rate, 26 per minute. The urine showed a 3 plus reaction for albumin and an occasional granular cast. The red blood cell count was 4,880,000. The hemoglobin content was 16 Gm. The white blood cell count was 10,000, with 68 per cent neutrophils, 29 per cent lymphocytes and 9 per cent monocytes. The blood sulfadiazine level was 14 mg per hundred cubic centimeters. A smear of material from the gums showed a few pus cells, a few fusiform bacilli and a moderate number of staphylococci.

During the hospital stay three cultures of material from the throat and mouth grew *Staphylococcus aureus* as the predominating organism. Three cultures of the blood were sterile after seventy-two hours. Heterophile antibody agglutinins for sheep cells were present in a titer of 1 to 40. The Kahn reaction of the blood was negative.

On the tenth day of illness the urine was normal. The red blood cell count was 4,120,000, the hemoglobin content, 14.8 Gm, and the white blood cell count, 4,200, with 56 per cent neutrophils, 39 per cent lymphocytes and 4 per cent monocytes.

During the second day of hospitalization the patient became mentally disoriented, restless and noisy. The taking of food, drink or medicaments induced vomiting. He had many involuntary liquid stools. At this time small bullous lesions were noted at the junction of the rectal skin and mucosa. The abdomen was tender generally and moderately distended. He had repeated chills. His temperature continued to range between 105.5 and 106.5 F, with a pulse rate of 120 and a respiratory rate of 20 to 30 per minute.

During the next three days no improvement was noted in his condition (which was extremely critical) except that eight hours after the use of penicillin was started (20,000 units every three hours) at the end of the seventh day of illness, there was a sharp drop in the temperature to 101.2 F and the pulse rate fell to 110 per minute.

On the eighth day there was evident coalescence of the lesions in the mouth and beginning rupture of the vesicles.

On the ninth day of illness a fine macular eruption developed over the trunk and extremities, which was more pronounced on the ventral surface. It was not pruritic. Improvement was first noted late on the tenth day of illness, when the patient was able to retain food. He was rational on the eleventh day.

By the twelfth day the rash was gone except on the lower abdominal wall. All the vesicles on the mucous surfaces of the mouth had ruptured, and the ulcerated surface was healing. The lips were dry and scaling except for areas in the midline on the lower lip and at the left labial angle, which were ulcerated. The patient took a soft diet and had a good day but was weak and tired.

He sat in a chair on the twenty-first day, had a normal stool on the twenty-second day and went home on the twenty-third day of illness, with normal temperature. The rash on the body was gone, and the buccal mucous membrane and tongue were practically free from ulceration.

*Treatment*—The treatment by the family physician before the patient's entrance to the hospital, as has been noted, consisted of the administration of sulfadiazine and the use of sodium perborate as a mouth wash and supportive measures. After hospitalization it seemed evident that no help was resulting from sulfadiazine, and its use was discontinued. On a purely empiric basis, penicillin was given intramuscularly for four days at the rate of 20,000 units every three hours and then every four hours for one day. A total of 760,000 units of penicillin was given. Other therapy was supportive and symptomatic.

#### COMMENT

This case presented nothing not mentioned in the literature of the past twenty-five years. Of outstanding note were the almost complete involvement of the buccal mucosa, the tongue and the lips, the continuous diarrhea and vomiting, which created an acute problem in fluid balance, body chemistry and nutrition, the severe disorientation and the appearance of imminent death, which lasted for days.

The dramatic drop in temperature and the rapidly ensuing recovery after the start of penicillin therapy seemed sufficiently significant to warrant reporting the observation.

#### SUMMARY

In a case of severe erythema multiforme treatment with penicillin seemed to be effective in initiating recovery.

# ALLERGIC REACTIONS DURING THE ADMINISTRATION OF PENICILLIN

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Any new medicine for general use which has the curative values attributed to penicillin and the almost complete lack of reports of reactions becomes a new agent for the treatment of many diseases without the fear that is attached to the use of the more toxic benzene ring derivatives such as the sulfonamide compounds, arsphenamine and others

However Jadassohn Schaaf and Sulzberger<sup>1</sup> and their collaborators found that the products of fungi were capable of producing anaphylactic shock in guinea pigs and found that the uterine horn of a guinea pig (Schultz-Dale reaction) was even sensitized by these extracts<sup>2</sup> They were also able to elicit immediate reactions in cutaneous sites passively sensitized by a previous injection of serum containing Prausnitz-Kustner antibodies to trichophyton

By the use of the Schultz-Dale phenomenon these investigators found that the extracts prepared from various species of dermatophytes showed a common antigenic factor It is now an ascertained fact that all extracts of the hyphomycetes contain in addition to the allergic reactions peculiar to each particular species, a powerful allergenic principle common to and characteristic of all

Dermatologists who are cognizant of the many explosive reactions from fungous toxins such as bullous eruption of the hands and feet generalized 'ids' erysipelas-like trichophytic manifestations and many others have watched with interest those patients who were being treated with the new drug penicillin

The sites in which the fungi usually manifest themselves have been carefully and frequently examined for evidence of any change in local tissue resistance or of allergic reactions to the common hyphomycetic allergin in penicillin

It has been my opportunity to observe 2 cases in which almost identical reactions occurred during the administration of penicillin

1 Jadassohn W, Schaaf F, and Sulzberger M B Der Schultz-Dalesche Versuch mit Trichophyton, Klin Wchnschr 11:857 1932

2 Jadassohn, W, Schaaf F, and Wohler G Analysis of Composite Antigens by the Schultz-Dale Technique Further Experimental Analysis of Trichophytins, J Immunol 32:203 1937

## REPORT OF CASES

CASE 1—L R, a white man 23 years old, was first seen by me on July 3, 1944 He reported that on May 1, 1944, because of a severe impaction, he had had the lower right third molar removed Within twenty-four hours after its removal he noticed swelling and pain in the right mandibular area which was controlled by sulfadiazine orally in doses of 60 grains (4 Gm) daily After three weeks of sulfadiazine therapy treatment was discontinued, and there was a relapse of the infection of the jaw The patient resumed taking sulfadiazine, in doses of 30 grains (2 Gm) daily, but this time there was no change in the tumor mass

Examination revealed a hard indurated swelling of the right submaxillary area at the angle of the mandible, about 2.5 cm in diameter Smears of material from this lesion revealed soft granules, which consisted of pure mats of radial filaments the size of actinomycetes but without the clubs Later, the typical sulfur granules of actinomycosis were found A diagnosis of actinomycosis was made Penicillin therapy was started immediately with filtered roentgen rays administered locally Penicillin in doses of 12,500 units was given every three hours, with some improvement but new areas developed above and below the lesion On the fifth day, after 400,000 units had been administered the patient complained of a vesicular eruption on the genitals and on the webs of the fingers This vesicular eruption spread to the crural region and about the scrotum The itching was severe.

A diagnosis of scabies was made and benzyl benzoate emulsion was applied three times with no improvement. Local applications of calamine lotion and hot packs of solution of boric acid were applied but failed to check the eruption The eruption about the fingers changed rapidly It first resembled a dyshidrotic type of fungous reaction But as it progressed, the eruption evolved into eczematous-like patches between the fingers and on the dorsa of the hands In the crural region there were a coalescence of the vesicles and a large area of maceration about both sides of the scrotum, similar to severe tinea cruris Sensitivity to penicillin was suspected and the use of the drug was discontinued Within twenty-four hours after the use of penicillin had been discontinued the eruption was exfoliating and the itching had ceased Further questioning revealed that the patient had never had dermatophytosis of the feet or any crural infection from fungus

Intradermal tests with 0.1 cc. of penicillin (500 units) revealed no immediate reaction or any reaction after ninety-six hours An intradermal test with trichophyton (1:30 dilution, 0.1 cc) elicited a negative reaction, but an intradermal test with oidiomycin (0.1 cc of a 1:100 dilution) was strongly positive in forty-eight hours Cultures of material from the areas were negative for fungi

A specimen of the urine showed a few leukocytes and crystals Complete blood counts were normal with the exception of an increased white cell count of 11,600

Six months following the acute dermatitis and the facial actinomycosis both of which were completely

cured, the patient returned with a recurrence of the margined pruritic eruption in the crural region, typical of tinea cruris. Microscopic examination of scrapings of skin from the lesions revealed hyphae which were typical in size and shape of those produced by pathogenic fungi. Cultures on Sabouraud's agar revealed a growth in twelve days of white fluffy colonies, which later turned slightly buff colored. These colonies were suggestive of *Trichophyton gypsum*, but the fungus was identified by Dr. Chester Emmons, mycologist of the



Fig 1—Eruption in the crural region with macerated area on the left side of the scrotum (case 2)

United States Public Health Service, Washington, D. C., as *Corethropsis*. Roentgen ray irradiation and local therapy promptly cleared the infection.

This case resembles the second case presented by Graves, Carpenter and Unangst,<sup>3</sup> in that the patient did not react to the intradermal test with penicillin. The eruption in this case may have resulted from toxins liberated from the actinomycetic infection by the penicillin or from such an alteration in the local immunity at the site of the eruption since the extract of 1:100 dilution from *Monilia albicans* elicited such a high degree of response that a monilial infection resulted locally, even though cultures were negative for the organism. With the recent appearance of dermatophytosis in the crural region, a loss of immunity to fungous organisms seems to be more probable.

CASE 2—M. T., a white man 36 years old, was admitted to the hospital for fever therapy. He had been treated for syphilis for one and a half years with the

3 Graves, W. N., Carpenter, C. C., and Unangst, R. W. Recurrent Vesicular Eruptions Appearing During Administration of Penicillin, *Arch Dermat & Syph* 50:6 (July) 1944.

routine type treatment of alternating courses of arsenicals and bismuth preparations, which had failed to produce a reversal of the Wassermann reaction of his blood. The Wassermann reaction of the spinal fluid was positive. After thirty-two hours of fever (temperature above 102 F) penicillin therapy was started, with 12,500 units given intramuscularly every three hours. After two doses were given, the patient noticed a vesicular eruption on the webs of the fingers and toes, on the penis and on the left inguinal area. There was no right testicle, hence the small vesicular lesions were limited to the left side of the crural region. The drug was continued for four days, and the itching became so severe that 1½ grains (90 mg) of pentobarbital sodium and ½ grain (30 mg) of codeine sulfate failed to give more than a few hours of relief.

The patient gave a history of dermatophytosis of the feet, but no diagnosis of tinea cruris had ever been made, although he admitted he had had some redness in the crural region and itching at times.

Examination at this time showed an area of erythema and maceration about the left crural region 7 cm in diameter with a demarcated border. At the edge of this large area there remained a roll of tissue 5 or 6 mm in width, which was a part of the epithelial roof of the large bulla. This was removed for sodium hydroxide preparations and for culture. The penis was covered with numerous vesicles and papules, and there were a few in the right inguinal region. Between the toes there was a moist denuded area with a bright red erythema spreading out on the dorsa of the feet from the webs of the toes. The eruption was similar to an erysipelas-like dermatophytosis. He also had a similar eruption between the fingers, which was vesicular, with spreading erythema on the dorsum of the hand. There was a mild erythematous, urticarial eruption about the forehead. An intradermal test was performed with 0.1 cc of freshly prepared penicillin containing 1,000 units. In thirty minutes there was a wheal reaction about the site, about 2 cm in diameter, which slowly faded. In sixty hours there developed a vesicle with



Fig 2—Raw denuded areas between the toes (case 2)

an erythematous base at the site of the injection. Tests with 0.1 cc of a 1:30 dilution of trichophytin (Lederle) and 0.1 cc of 1:100 dilution of oidiomycin (Lederle) failed to elicit any response. As a control 10 other patients were given intradermal injections of 1,000 units of penicillin, and no reaction was elicited in any case.

Microscopic examination of the roof of the bulla from the crural region when dissolved in 10 per cent solution of sodium hydroxide revealed numerous mosaic fungi of various shapes. Several long hyphae were also

found, which in size and shape were typical of those produced by pathogenic fungi. Cultures on Sabouraud's agar slants failed to reveal any growths after four weeks of observation.

Cultures on blood agar plates revealed the presence of both *Staphylococcus aureus* and hemolytic streptococci. Cultures of blood showed no growth in five days. Complete blood counts were within the normal range. The Wassermann reaction of the blood was repeatedly positive, although at the time of discharge the Wassermann reaction of the spinal fluid was negative. Urine specimens contained no sugar and no albumin. The fasting blood sugar level was 105 mg per hundred cubic centimeters of blood.

The pruritus abated promptly after penicillin therapy was stopped, but the eruption did not clear until ten days later. Treatment consisted of local therapy with 2 per cent aqueous solution of gentian violet medicinal, moist packs of calamine lotion and baths in a weak solution of potassium permanganate (1:15,000).

#### COMMENT

Graves, Carpenter and Unangst<sup>3</sup> have reported 2 cases in which an eruption of a recurrent vesicular nature occurred during the administration of penicillin. They suggested that it was a manifestation of sensitization to penicillin or to the contained substances employed in its manufacture. This concept is probably the correct one. They also considered that the dyshidrosiform lesions might result from toxins, liberated by foci of infection, to which the patient was sensitive. There is the possibility that other factors enter into the cause of the reactions. There should be considered the possibility of an alteration of the local immune factors in areas of skin which harbor other fungous spores, allowing them to become active. In the second case presented I was able to find numerous mosaic fungi and a few true hyphae, although cultures failed to reveal any growth of pathogenic fungi. The fact that the eruption in both cases was in areas favorable to the growth of fungi, i. e., the crural region and the webs of the toes and fingers, seems to favor some alteration of local immune balance.

The vesiculobullous reaction at the site of the injection of 1,000 units of penicillin in case 2, however, seemed to bear out the original concept of Graves, Carpenter and Unangst<sup>3</sup>.

What the allergic principle may be is a matter of conjecture. Bloch, Labouchère and Schaff<sup>4</sup> and Jadassohn and collaborators in their studies of the polysaccharide fractions of various strains of fungi, concluded that they still represented

a complexity of different allergenic and partially antigenic properties. Some of these haptens were able to produce specific sensitivities. I am led to believe that the allergenic principles in penicillin are in all probability a polysaccharide fraction.

One further case of allergy to penicillin has been reported by Criepp<sup>5</sup>. His patient showed an acquired sensitivity to penicillin analogous to drug or serum allergy. The patient exhibited an urticarial reaction as soon as the injection of penicillin was made. The reaction continued until the penicillin therapy was discontinued. Precipitin tests with the patient's serum and penicillin elicited positive reactions, while tests with control serums elicited negative reactions.

The following principles were concluded from the observations made during the administration of penicillin.

- 1 Patients selected for treatment with penicillin should be carefully questioned about previous reactions to fungi, such as bullous eruption of the hands and feet caused by fungi, severe eczematous "ids" or others of the more severe manifestations of a mycotic nature.

- 2 Patients reporting reactions to fungi should be tested with from 500 to 1,000 units of penicillin intradermally. If a bullous lesion appears at the site of injection, extreme caution should be used in the administration of the penicillin.

- 3 If a history of chronic fungous infection is elicited, during the administration of penicillin great care should be given to the areas subject to mycotic infection: baths in a weak solution of potassium permanganate (1:15,000), thorough drying after bathing and use of a mild dusting powder, consisting of 10 parts of boric acid, 45 parts of talc and 45 parts of zinc oxide powder, locally about the genitocrural regions and between the fingers and toes.

#### SUMMARY

Two cases of vesicular eruption to penicillin occurred. Neither reaction was of serious consequence except that discontinuance of the drug became necessary because of extreme pruritus from the eruption.

Suggestions for the prevention of such reactions in the future include careful questioning of patients regarding previous reactions to fungi, administration of an intradermal test with 500 to 1,000 units of penicillin and special local care of areas subject to mycotic infection.

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<sup>5</sup> Criepp, L. H. Allergy to Penicillin, *J A M A* 126:429 (Oct 14) 1944.

# PENETRATION OF SURFACE TISSUES WITH COPPER BY IONTOPHORESIS

PENETRATION WITH ORGANIC AND INORGANIC COPPER SALTS AND  
THE USE OF DETERGENTS IN IONTOPHORESIS

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Iontophoresis, the introduction of ions of electrolytic salts into the tissues of the body for therapeutic purposes by means of the galvanic current, was developed as a method of treatment during the latter part of the nineteenth century. The experiments carried out with iontophoresis in animals and in human beings by Leduc at the turn of the century helped to create new applications in this field of therapy.<sup>1</sup> Since its introduction, this procedure, also referred to as medical ionization or ion transfer, has been tried in the treatment of almost every accessible surface tissue in the body, notably in the eyes,<sup>2</sup> the nose,<sup>3</sup> the ears,<sup>4</sup> the skin,<sup>5</sup> the teeth<sup>6</sup> and

genital tissues.<sup>7</sup> Notwithstanding the long period of clinical trial, the value of iontophoresis as a method of increasing the penetration of therapeutic substances through the intact surface membranes of the body has continued to remain a matter of dispute.

In the case of organic salts, the physiologic reactions evoked in the body by their introduction into the tissue provide a measure of the degree of penetration attained and of the efficacy of iontophoretic treatment. Early in the investigations of this procedure, Leduc described the passage of lethal amounts of strychnine and of cyanides through the intact skin of rabbits by iontophoresis. Many organic compounds have been successfully applied therapeutically by this method of treatment and their use in this way has been reported in the literature. Among these are atropine and scopolamine,<sup>8</sup> epinephrine,<sup>9</sup> physostigmine,<sup>10</sup> procaine,<sup>11</sup> histamine<sup>12</sup> and

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mecholy<sup>13</sup> More recently, the sulfonamide compounds<sup>14</sup> and the sodium salts of penicillin have been introduced into the eye by iontophoresis<sup>15</sup> Sodium penicillin has been found to migrate readily through human skin and mucous membrane under the influence of the galvanic current<sup>16</sup> Without the current, the amounts of these organic salts which may be introduced into the body are comparatively small

In the case of the inorganic salts of metals, such as have been used extensively in the past in iontophoretic treatment, the evidence in support of an increased penetration of body tissue by these metal ions through the use of the galvanic current has not been convincing Inasmuch as many of these metal salts may be detected in tissue sections by special staining reactions, a proper evaluation of the penetration of tissues by such salts with iontophoresis would reasonably require their demonstration within the treated tissues A review of the literature on this subject fails to reveal substantial evidence of penetration of surface tissues by these metal salts through use of the galvanic current Baker,<sup>17</sup> in a critical examination of the subject called attention to the limited penetration of the superficial epithelium in surface membranes which has been observed after iontophoresis with metal salts Turrell<sup>18</sup> spoke of the fallacy of deep ionic medication The Council of Physical Therapy of the American Medical Association

in 1939<sup>19</sup> concluded that the inability to demonstrate penetration of metal ions in tissues treated with metal salts by iontophoresis may be due to two reasons first, that the metal ions are precipitated by the tissue proteins on the surface of the tissue and are thus bound and prevented from penetrating the tissue further and, second, that while the metal ions may permeate the surface tissues, they may be removed by the circulation too rapidly to be demonstrated on histologic examination

The experiments to be described are intended to show that

1 Copper sulfate in aqueous solution used in the treatment of mucous genital tissue is not substantially more penetrating when applied with the galvanic current than when used without the current The current applied to solutions of copper sulfate alone only produced heavier deposits of copper in the surface epithelium

2 Deep penetration of copper ions into mucous genital tissue can be effected through the use of certain synthetic wetting agents or detergents applied in solution with the copper sulfate by iontophoresis Deep penetration was not obtained without the use of the current

3 Maximum penetration of copper into mucous genital tissue can be obtained through the use of organic salts of copper by iontophoresis Without the current, the penetration of copper in the tissue in this organometallic form was superficial

4 The binding of copper by tissue proteins bars the penetration of this metal into surface tissues in iontophoresis This chemical reaction of copper ions and proteins was inhibited to a limited extent in vitro by certain synthetic detergents, it was prevented completely by incorporation of the copper into organic compounds

#### TECHNIC

These tests were carried out on the rabbit penis Mucous genital tissue was selected in preference to skin because of the uniformity of surface provided The skin, through the hair follicles present, offered access to the deeper layers of tissue, so that a correct evaluation of the depth of penetration obtained by copper was impossible In order to extend the penis and to provide a maximum mucous surface for iontophoretic treatment, a glass exposure chamber was devised as shown in the diagram (fig 1)

This chamber was prepared from a 10 cc serum bottle (Kimble brand) The base of the ampule and the stem were ground off to give the dimensions indicated The narrow end of the glass chamber fitted the width of the penis when this was extended through it The opposite end of the chamber was provided

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with a rubber stopper through which a hypodermic needle was introduced. A Luer-Lok stopcock was inserted in the hub of this needle.

In use, the narrow stem opening of the chamber was placed over the rabbit penis. A reduced atmospheric pressure was then produced in the chamber by drawing back the plunger of a 10 cc syringe inserted in the stopcock. This reduced pressure served to draw the penis into the chamber. Copper solutions were introduced into the chamber through the stopcock and needle with the syringe, the vacuum present in the chamber drawing the solutions into the chamber automatically. After the negative pressure in the chamber was reestablished with the syringe, the stopcock was closed. The penis remained extended in the solution in the glass chamber during exposure to treatment by means of the partial vacuum thus retained in the chamber (approximately 5 cm of mercury).

The needle in the chamber was kept immersed in the solutions but was removed from contact with the penis. The lead from the positive source of current was connected to the hub of the needle. The negative lead was connected to a needle introduced subcutaneously into the thigh of the rabbit. The flow of current was controlled with a rheostat and measured by a milliammeter placed in series.<sup>20</sup>

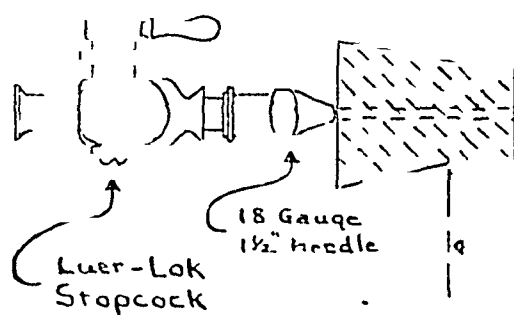


Fig 1—Glass exposure chamber

For comparative studies, the strength of the copper solutions used, the amount of the current applied and length of iontophoretic treatment given were standardized, so that 1 per cent solutions were employed regularly in tests with a 5 milliamper current for fifteen minutes. Immediately after treatment, the animal was killed, and the penis was amputated. The tissue was placed in 95 per cent ethyl alcohol and was prepared, sectioned and stained for copper in accordance with the Mallory technic.<sup>21</sup> The effect of the current itself on the staining reaction in the tissue was tested by treating tissues with a 1 per cent sodium sulfate solution by iontophoresis under the same conditions used in the copper-treated tissues. It was shown that the current does not produce changes in the tissue to give the blue color reaction which characterized the tissue sections containing copper.<sup>22</sup>

20 An Ionophore Unit was provided for these experiments by the Burdick Corporation, of Wisconsin.

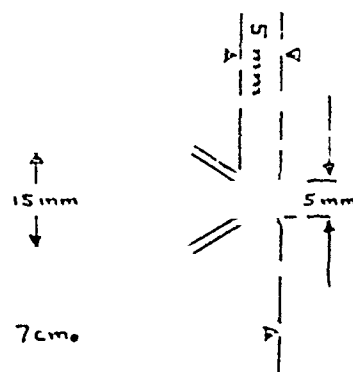
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22 Tissue sections were prepared by Miss Alice Malloy, senior medical technician, United States Marine Hospital Staten Island, N Y.

## I. PENETRATION OF INORGANIC SALTS OF COPPER

With the technic just described, experiments were carried out to test the penetration of copper into the rabbit penis from aqueous cupric sulfate solution, with and without current. Exposures to solutions of copper sulfate were first carried out. When iontophoresis was employed 5 milliamperes of current was used during the entire period of exposure.

The treated tissues were recovered, prepared, sectioned and stained for copper. The sections were obtained at different levels along the shaft of the penis, each a complete cross section of the tissue. A typical cross section of rabbit penis treated with a 1 per cent aqueous cupric sulfate solution for fifteen minutes without current when examined under the microscope showed superficial irregular deposits of copper on the surface epithelium. The copper did not



penetrate through the epithelial layer of the penile mucosa.

The sections of penile tissue treated with 1 per cent copper sulfate solution by iontophoresis showed a more uniform deposit of copper on the surface epithelium. While the density of the copper appeared slightly greater in such sections, the depth of penetration of the copper into the tissue was not substantially increased. Again, only a thin layer of copper was found deposited on the surface epithelium, and the subepithelial tissue was not invaded by the copper.

An increase in the duration of treatment to thirty minutes with a 5 milliamper current being used or an increase in the amount of current to 10 milliamperes for fifteen minutes resulted in a heavier deposit of copper on the surface. The depth of penetration of copper into the tissue, however, was equally shallow.



On gross examination, the penile tissue treated with copper sulfate by iontophoresis showed a thin deposit of copper on the surface which was not readily removed by washing with water or rubbing, the copper appeared bound to the mucosa.

The effect of reversal of current on penetration of copper into the rabbit penis by iontophoresis was tested on several animals. The penis of each rabbit was exposed to a 1 per cent copper sulfate solution in the glass chamber for fifteen minutes by iontophoresis with a

ness of the surface epithelium. The density of copper deposited in the surface epithelium appeared the same as that obtained in fifteen minutes with the positive electrode alone in the copper sulfate solution.

The maximum depth of penetration by copper in the rabbit penis treated with copper sulfate with the galvanic current was not substantially greater than that obtained without the current. The density of copper deposited in the surface epithelium was increased by using iontophoresis. The amount of this electrodeposition of copper

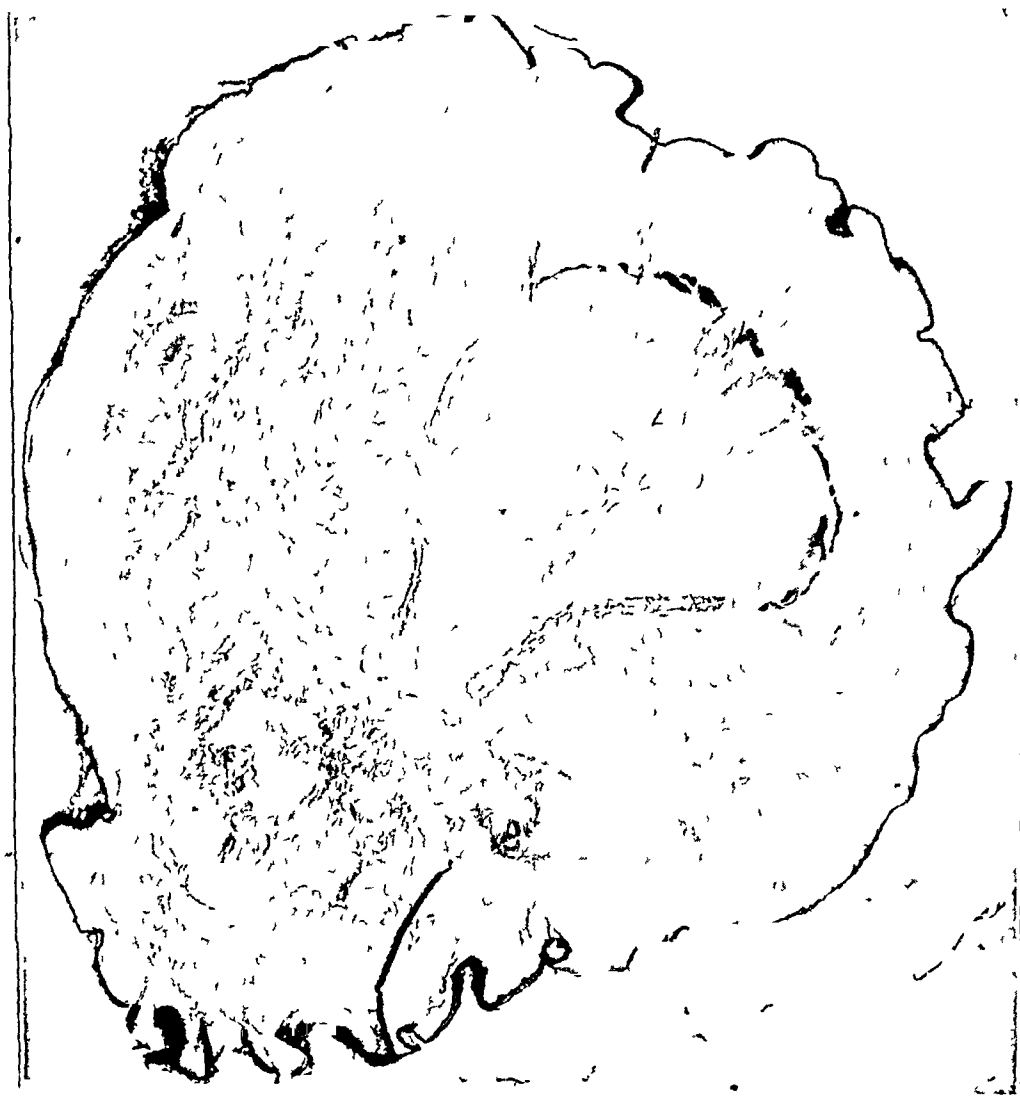


Fig 2—Penetration of copper after treatment with 1 per cent copper sulfate solution for fifteen minutes by iontophoresis with 5 milliamperes current

5 millampere current with the negative electrode in the solution. At the end of this time, the current was reversed, so that the electrode in the solution was connected to the positive terminal of the current. Five milliamperes of current was again applied for fifteen minutes.

Sections of tissues treated by this technic did not show greater depth of penetration of copper than was obtained in tissues treated for fifteen minutes with the positive electrode alone in the solution. The copper in tissues treated by this method permeated at most the full thick-

ness of the surface epithelium. The use of the negative electrode in the copper sulfate solution before applying the positive electrode to the solution did not result in appreciably greater increases in the amount of copper deposited by iontophoresis.

The copper deposited in the surface epithelium by the current was fixed to the tissue and persisted in situ. The copper deposited on the surface of the rabbit penis after exposure to



copper sulfate solution without the current was light in amount and was not firmly bound to the surface. Irritation of the tissue treated with copper sulfate by iontophoresis was considerably greater and the effects of the persistent copper on the tissue were more extensive and prolonged (fig 2).

## II PENETRATION OF COPPER BY IONTOPHORESIS WITH DETERGENTS

The effect of incorporating synthetic surface-active detergents with copper sulfate in solution on the penetration of copper into the penis of the rabbit by iontophoresis was investigated. Various types of these compounds were mixed with copper sulfate in aqueous solution to give a 1 per cent concentration of each. Those compounds which were found compatible with copper sulfate were tested on the rabbit penis for penetration of copper by iontophoresis. Tests were made with mixtures of the copper sulfate and the detergents in the glass exposure chamber for fifteen minutes with a 5 milliamperere current.

From the group of compounds investigated, three wetting agents were found which furthered the penetration of copper into the penis of the rabbit. Each of these was an anionic agent: (a) aerosol MA (dihexyl sodium sulfosuccinate), (b) aerosol AY (diamyl sodium sulfosuccinate) and (c) duponol C (primarily sodium laurylsulfate). These compounds used in 1 per cent concentration in solution with the copper sulfate produced considerably greater penetration of copper into the rabbit penis by iontophoresis. The subepithelial tissue of the penis was deeply penetrated by the copper. Without the galvanic current, penetration of copper from such mixtures of copper sulfate and detergent into the tissue was superficial. None of the cationic detergents tested<sup>23</sup> increased the penetration of copper in the tissue.

The sections of tissues treated with copper sulfate and aerosol MA showed a concentric layer of copper extending from the surface epithelium into the subepithelial tissue. The depth to which the copper penetrated was fairly uniform on all sides and showed a rather sharp internal delimitation. The depth of penetration of copper by iontophoresis with copper sulfate-aerosol MA solutions was approximately twenty-five times the depth of penetration of copper obtained by iontophoresis with copper sulfate alone. When the length of iontophoretic

treatment with the copper sulfate-detergent solutions was increased from fifteen minutes to thirty minutes, the concentration of copper in the tissue was increased, but the depth of penetration by the metal was only slightly changed. The amount of copper introduced from such mixed solution was also increased by applying a current of 10 milliamperes, instead of 5 milliamperes, for fifteen minutes. The depth of penetration by copper under either condition was not significantly increased.

The effect of reversal of current on the penetration of copper from copper sulfate-detergent solutions in iontophoresis was tested on the rabbit penis. The negative electrode was applied to 1 per cent copper sulfate-aerosol MA solution for fifteen minutes. Iontophoretic treatment of the penis was given with a 5 milliamperere current. The current was then reversed, so that the positive electrode was in the solution, and a current of 5 milliamperes was applied for fifteen minutes.

The sections of tissue treated by iontophoresis in this manner revealed a heavy concentration of copper deep in the tissue. The amount of copper introduced into the penis by reversing the current during iontophoretic treatment was only slightly greater than the amount of copper introduced with this copper sulfate-aerosol MA solution by iontophoresis with the positive pole alone applied to the solution for thirty minutes. The copper in these sections was present as a solid concentric ring pervading the surface epithelium and the subepithelial structures. The depth of penetration of copper beneath the surface in these tissues treated with copper sulfate and aerosol MA was more than twice the depth of penetration of copper obtained with this same preparation in tissues treated by iontophoresis with the positive electrode used alone for thirty minutes in the solution (fig 3). With the negative electrode alone applied to the copper sulfate-aerosol MA solution for thirty minutes with a 5 milliamperere current, the penetration of copper into the penis was shallow.

The effect of decreasing the concentration of the detergent added to the solution of copper sulfate on penetration of copper into tissue by iontophoresis was investigated. A 1 per cent copper sulfate solution with only 0.5 per cent aerosol MA was prepared and used to treat the rabbit penis by iontophoresis for fifteen minutes. The tissues treated with this solution showed almost exactly one half the depth of penetration and one half the amount of copper introduced into the tissue compared with that obtained with 1 per cent aerosol MA.

23 Other detergents tested and found ineffective included aerosols 18, 1 B, 22, OS and OT, Pegm Nacconal, Acidolate, Tergitol Penetrant no 7, glycerol monostearate S, Intracol S, Santomerse 3, Carbitol, and quarternary ammonium compounds.

III PENETRATION OF ORGANIC  
SALTS OF COPPER

The effectiveness of iontophoresis in increasing penetration of copper from solutions of organic salts of this metal into the rabbit penis was investigated. Three organic salts of copper were prepared<sup>24</sup> in aqueous solution by mixing copper sulfate with organic salts to yield (a) bis-(trimethylenediamino) cupric sulfate, (b) ethylenediamine cupric sulfate and (c) triethanolamine cupric sulfate. The copper ions were incorporated in the organic molecule to yield color changes in

recovered and the sections prepared and stained as before.

Sections of tissues treated by these organic copper salts showed deep, diffuse penetration of copper. In each specimen, the entire cross section of the tissue was found to be permeated with copper. The distribution of copper in the tissue was uniform throughout, the heavier concentration of copper observed in the epithelial layer with iontophoresis of copper sulfate-aerosol MA solution was lacking. The sharp line of demarcation found in tissues treated with cop-

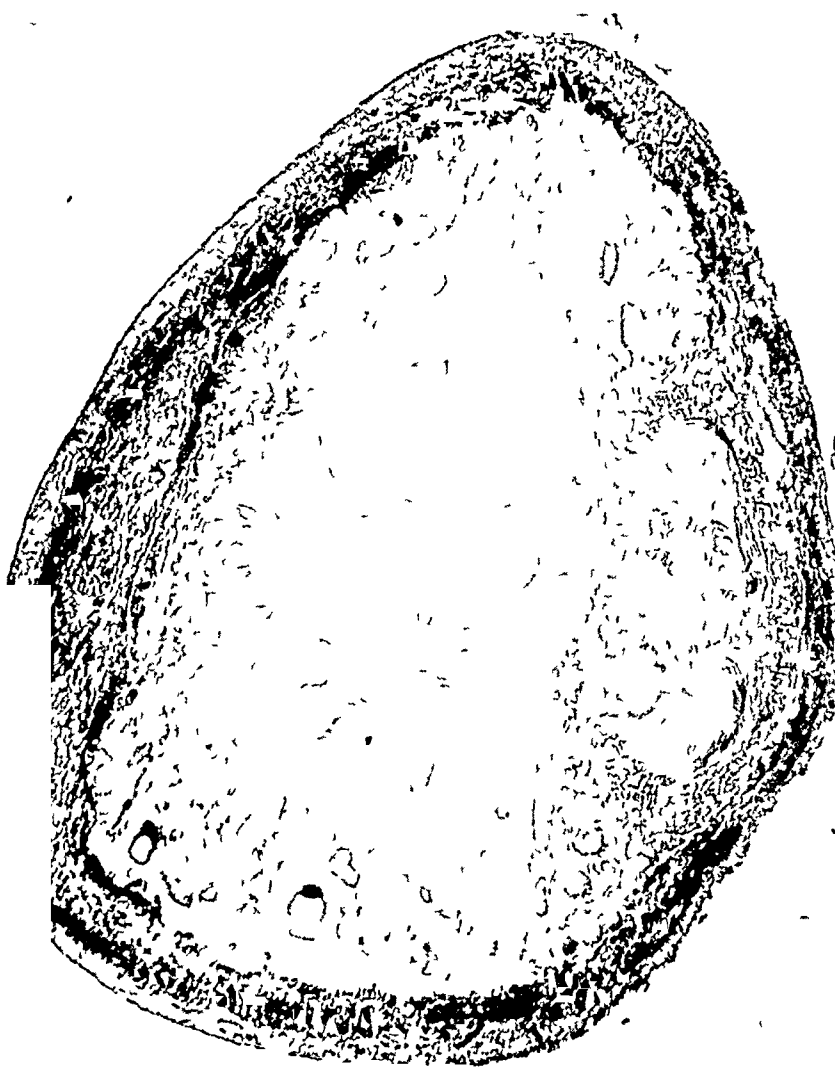


Fig 3—Penetration of copper after treatment with a solution of 1 per cent copper sulfate and 1 per cent aerosol MA for fifteen minutes by iontophoresis with 5 milliamperes current

solution distinct from the usual light green color of copper sulfate solutions.

Each of these organic copper salt solutions in 1 per cent concentration was tested for penetration into the rabbit penis in the glass exposure chamber by iontophoresis with a 5 milliampere current for fifteen minutes. The tissues were

per sulfate-aerosol MA solution showing the limits of penetration of copper into the tissue was absent in the tissues treated with these organic copper salts.

Control experiments were done to test the penetration of these organic copper salts into the rabbit penis exposed to solutions of these salts in the glass chamber for fifteen minutes without the use of the current. Sections of these control tissues did not reveal any penetration by copper. Only a light irregular deposit of copper was found on the superficial epithelium.

<sup>24</sup> Compounds were prepared by Lawrence H. Amundsen and Lena A. Malentacchi, of the department of chemistry of the Venereal Disease Research Laboratory, United States Marine Hospital, Staten Island, N. Y.

When the length of iontophoretic treatment of the rabbit penis with these organic salts was increased from fifteen to thirty minutes, the concentration of copper throughout the sections

duced a higher concentration of copper in the tissues. By the technic of reversing the current that was used previously, the amount of copper introduced in the tissues treated with these

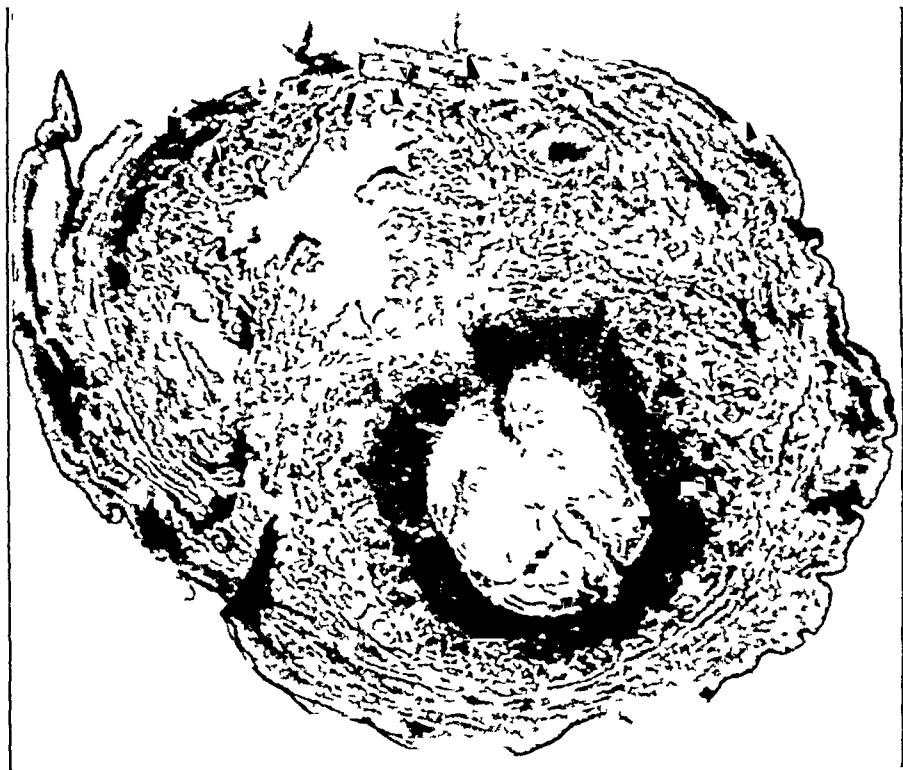


Fig 4—Penetration of copper after treatment with 1 per cent bis(trimethylenediamino)copper sulfate for fifteen minutes by iontophoresis with 5 milliamperes current

Penetration of Copper in Penis Tissue of Rabbits

| Solution |  | Milli<br>amperes | Electrode<br>Applied to<br>Solution | Duration<br>of<br>Treatment,<br>Minutes | Surface<br>Area<br>Treated,*<br>Sq. Mm. | Amount of<br>Copper in<br>Tissue *<br>Mg. | Depth of<br>Copper<br>Penetration,<br>Mm. |
|----------|--|------------------|-------------------------------------|---|---|---|---|
| 1        | 1% copper sulfate †                            | None             | None                                | 15                                      | 114                                     | 0.00                                      | 0.011                                     |
| 2        | 1% copper sulfate                              | 5                | Positive                            | 15                                      | 151                                     | 0.13                                      | 0.011                                     |
| 3        | 1% copper sulfate                              | 5                | Positive                            | 30                                      | 157                                     | 0.50                                      | 0.120                                     |
| 4        | 1% copper sulfate                              | 10               | Positive                            | 15                                      | 157                                     | 0.623                                     | 0.140                                     |
| 5        | 1% copper sulfate                              | 5                | Negative                            | 15                                      |   |   |   |
|          |  | 5                | Positive                            | 15                                      | 165                                     | 0.473                                     | 0.140                                     |
| 6        | 1% CuSO <sub>4</sub> + 1% aerosol MA           | None             | None                                | 15                                      | 131                                     | 0.071                                     | 0.021                                     |
| 7        | 1% CuSO <sub>4</sub> + 1% aerosol MA           | 5                | Positive                            | 15                                      | 80                                      | 0.44                                      | 0.280                                     |
| 8        | 1% CuSO <sub>4</sub> + 1% aerosol MA           | 5                | Positive                            | 30                                      | 102                                     | 0.73                                      | 0.350                                     |
| 9        | 1% CuSO <sub>4</sub> + 1% aerosol MA           | 10               | Positive                            | 15                                      | 118                                     | 0.59                                      | 0.560                                     |
| 10       | 1% CuSO <sub>4</sub> + 1% aerosol MA           | 5                | Negative                            | 15                                      |   |   |   |
|          |  | 5                | Positive                            | 15                                      | 139                                     | 0.76                                      | 0.540                                     |
| 11       | 1% CuSO <sub>4</sub> + 0.5% aerosol MA         | 5                | Positive                            | 15                                      | 132                                     | 0.23                                      | 0.140                                     |
| 12       | 1% bis(trimethylenediamine)CuSO <sub>4</sub> ‡ | None             | None                                | 15                                      | 104                                     | 0.00                                      | 0.000                                     |
| 13       | 1% bis(trimethylenediamine)CuSO <sub>4</sub>   | 5                | Positive                            | 15                                      | 148                                     | 0.407                                     | 2.520                                     |
| 14       | 1% bis(trimethylenediamine)CuSO <sub>4</sub>   | 5                | Positive                            | 30                                      | 176                                     | 0.717                                     | 2.380                                     |
| 15       | 1% bis(trimethylenediamine)CuSO <sub>4</sub>   | 10               | Positive                            | 15                                      | 173                                     | 0.83                                      | 2.450                                     |
| 16       | 1% bis(trimethylenediamine)CuSO <sub>4</sub>   | 5                | Negative                            | 15                                      |   |   |   |
|          |  | 5                | Positive                            | 15                                      | 162                                     | 0.493                                     | 2.380                                     |

\* The amounts shown in the last three columns represent the average measurements in each group of 4 rabbits tested.  
† All of the copper in tissues treated with solutions 1 to 5 above was present on the superficial epithelium only.  
‡ The depth of penetration of copper with bis(trimethylenediamine)copper sulfate was maximal in each tissue. The entire cross section of penis was permeated by copper in solutions 13 to 16. The figures on penetration in these tissues indicate the thickness of the penis from center to the surface epithelium.

of these tissues was increased. An increase in the amount of current applied in fifteen minutes from 5 to 10 milliamperes likewise pro-

duced approximately the same as that obtained by use of the positive electrode alone in the organic

copper salt solution for fifteen minutes. The depth of penetration of copper with these organic copper salts was maximal under each of the conditions tested (fig 4)

#### IV QUANTITATIVE DETERMINATIONS OF COPPER IN TREATED TISSUE

The quantities of copper introduced into the rabbit penis by the different methods of application tested and with the three types of solutions are analyzed in the table. The surface area of the penis through which these quantities of copper were introduced into the tissues was measured by making a collodion cast of each penis. After drying, the collodion film was cut lengthwise, removed immediately and spread on a millimeter graph. The area covered on the graph was measured directly to give the area of tissue surface treated. The tissues were reduced to ash, and quantitative determinations of the amount of copper present in each tissue was determined separately by the method of Eden and Green<sup>25</sup>. A minimum of 4 rabbits was used in determining the depth of penetration of copper and the amount of copper in the penis under each of the conditions listed<sup>26</sup>.

#### V THE ROLE OF TISSUE PROTEINS IN PENETRATION OF COPPER

It may be postulated that the decided difference observed in the depth and in the amount of penetration of copper obtained in the rabbit penis by iontophoresis with copper sulfate alone, with copper sulfate-aerosol MA solution and with organic copper solutions is based on differences in chemical reactivity between these solutions and the surface tissues. The precipitation of metals by tissue proteins has been commented on previously in the literature. That the greater ability of copper to penetrate tissue by iontophoresis with copper sulfate-aerosol MA solutions and with organic copper salts than with copper sulfate alone is dependent on an inhibition or prevention of the chemical reaction between copper and tissue proteins appears to be manifested by the following *in vitro* tests.

A suspension of tissue proteins in an isotonic solution of sodium chloride was prepared from freshly circumcised human foreskins. The tissues were weighed and triturated with sand. The isotonic solution of sodium chloride was added to the triturated tissue in the

proportion of 2 cc of solution for each gram of tissue. The mixture was centrifuged, and the supernatant fluid was removed. A Kjeldahl determination was made on this solution. Nitrogen equivalent to approximately 0.38 per cent protein was found in the solution.

One cubic centimeter amounts of this solution, containing approximately 3.8 mg of protein, were placed in test tubes. To each of these tubes, 0.1 cc of 1 per cent copper sulfate solution, containing approximately 10 mg of copper sulfate, was added. The copper and the protein reacted immediately to form an insoluble precipitate.

A solution containing 1 per cent copper sulfate and 1 per cent aerosol MA was prepared, and 0.1 cc, containing approximately 10 mg of each, was added slowly to 1 cc amounts of the protein suspension in test tubes. The copper and protein did not react to form a precipitate. When more than 0.1 cc of this mixture was added, however, precipitation of protein by copper resulted immediately.

Aerosol AY was substituted for aerosol MA in the same tests and was found equally effective in preventing the precipitation of protein by copper to the same degree under the same conditions. Duponol C was found optimally effective in preventing the reaction of copper and protein in the same proportions with a concentration of this detergent of 0.5 per cent in solution. Five milligrams of this compound prevented the reaction of 10 mg of copper with 3.8 mg of protein. In each case, if more than 10 mg of copper sulfate was added to the protein-detergent mixtures the detergent was unable to prevent the reaction of copper and protein. These detergents were equally effective in preventing precipitation of copper proteinate if added to the protein solutions prior to the addition of the copper sulfate.

One per cent solutions of the organometallic salts bis(trimethylenediamino) copper sulfate, ethylenediamine copper sulfate and triethanolamine copper sulfate were tested with protein suspensions in the test tube. One cubic centimeter amounts of each of these solutions of organic copper salts were added to 1 cc amounts of the protein suspension. The protein in the test tubes was not precipitated by any of these organic copper salts even when added in excess to each cubic centimeter of protein suspension.

#### COMMENT

Copper sulfate has been used for many years in the treatment of diseased surface tissues by iontophoresis. The question whether copper applied by this method is more penetrating to the tissues than that used topically has not been satisfactorily answered. The observations reported here show that copper is not substantially more penetrating when applied in an aqueous copper sulfate solution with the current than it is without the current. The surface membrane of living tissue was found to resist the introduction of copper. A galvanic current applied to solutions of copper sulfate on mucous genital tissues of rabbits increased the amount of copper deposited and fixed on the surface but did not increase substantially the depth of copper introduced into the tissue.

<sup>25</sup> Eden, A., and Green, H. H. Microdetermination of Copper in Biological Material, *Biochem J* 34 1202-1208 (Sept.) 1940.

<sup>26</sup> Quantitative determinations of copper were made by T. V. Letonoff, associate research chemist, Venereal Disease Research Laboratory, United States Marine Hospital, Staten Island, N. Y.

The experiments reported in this study show that the resistance of the tissue to the penetration of copper is due in large part to the precipitation of this metal by the tissue proteins. Deep penetration of copper was obtained with iontophoresis, however, by prevention of this reaction of copper and protein. This was accomplished either by adding certain anionic detergents to the copper sulfate solution or by incorporating the copper into certain organic salts. On the one hand, the detergents used bound the tissue protein, so that a chemical union of copper and protein was inhibited. On the other hand, the organic salts bound the copper, so that the proteins did not react with the copper. It is considered that the detergents reacted with the proteins to form soluble complexes similar to those described by Anson<sup>27</sup> and by Putnam and Neurath<sup>28</sup>.

Of the two solutions found to be effective in introducing copper into tissue by iontophoresis, the organic copper was much more penetrating than the copper sulfate-detergent solutions. At the same time, the organic copper was less irritating to the tissue. It was observed that the organic copper was absorbed more rapidly and disappeared from the treated tissue within three hours after iontophoresis. Copper introduced into tissue by iontophoresis from copper sulfate-detergent solutions remained in the tissue and was demonstrated in tissue sections as late as twenty-four hours after treatment.

It is evident that a prolonged therapeutic action by copper locally in the tissue is possible after iontophoresis with either of the aforementioned copper solutions. It is likewise evident that this therapeutic effect may be produced much more deeply in the tissue with iontophoresis of these compounds than is possible with topical application. By applying these copper preparations to tissue with the galvanic current, true iontophoresis—that is, the transfer of copper through the surface and into the tissue by the current—is readily accomplished. These results are in decided contrast to the simple electrodeposition of copper on the tissue surface by the galvanic current observed when copper sulfate was used alone in solution.

The transport of copper ions into tissue by iontophoresis of copper sulfate-detergent mix-

tures or of organic copper sulfate salts is obtained only from aqueous solutions of these compounds. Attempts to introduce copper into tissue by iontophoresis of ointments containing the same copper preparations failed. The ointments were prepared from ammonium stearate or tragacanth jelly bases.

Limited tests were carried out *in vitro* to determine the bactericidal value of two of the copper salt preparations used in these experiments. Bis(trimethylenediamino)copper sulfate was found to have approximately one-tenth the germicidal value of copper sulfate. This organic copper salt, though less germicidal than copper sulfate, provides much deeper action by copper in surface tissues treated with this compound by iontophoresis. The chemical characteristics of bis(trimethylenediamino)copper sulfate originally prepared by Amundsen and Malentacchi for these experiments are reported elsewhere.<sup>29</sup> The second preparation tested consisted of copper sulfate and aerosol MA in equal concentration in aqueous solution. This combination was found to be as bactericidal as copper sulfate used alone. The greater toxicity of copper sulfate-aerosol MA to tissue, however, precludes use of this compound by iontophoresis in the same strength as copper sulfate alone.

In view of the delay in absorption of copper from tissue treated with solutions of copper sulfate-aerosol MA by iontophoresis which was observed in these experiments, repeated treatments with this preparation to the same tissue must be spaced sufficiently to avoid cumulative effects. The frequency of iontophoretic treatments when employing either the organic copper salt or copper sulfate-aerosol MA solutions over large tissue surfaces must be controlled to prevent toxic effects by the copper absorbed into the body on the internal organs.

With regard to the purported greater efficacy of copper sulfate applied by itself in the past by iontophoresis in the treatment of diseased surface tissues, it is questionable whether the benefits reported were due to actual transfer of copper inside the tissue by the galvanic current. Since the depth of penetration of copper in tissue treated with copper sulfate alone in solution by iontophoresis was shown in these experiments not to be substantially greater than the depth of copper penetration obtainable by topical application, the increased therapeutic value attributed to this salt when applied with the galvanic current may be explained as being

27 Anson, M. L. Denaturation of Proteins by Synthetic Detergents and Bile Salts, *J. Gen. Physiol.* **23** 239-246 (Nov) 1939.

28 Putnam, F. W., and Neurath, H. Complex Formation Between Synthetic Detergents and Proteins. Letters to the Editors, *J. Biol. Chem.* **150** 263-264 (Sept) 1943.

29 Amundsen, L. H., and Malentacchi, L. A. Bis-(Trimethylene diamino)Cupric Sulphate, *J. Am. Chem. Soc.* **67** 493 (April) 1945.

due possibly to the larger amounts of copper deposited on the surface and fixed on the tissue by the current, or it may be due to effects of the current itself on the tissue and on the copper sulfate solution

Insofar as the effects of the copper itself is concerned, the increased deposit of this metal on the tissue surface produced through use of the current may well serve to prolong the therapeutic action of the copper on the superficial tissue. With respect to the effects of the current on the tissue, Molitor and Fernandez<sup>30</sup> have reported changes in the hydrogen ion concentration of surface tissues treated by iontophoresis. In addition, tests made on the copper sulfate solutions used in the experiments reported here showed that considerable changes were produced by the current in the hydrogen ion concentration of these solutions. Vasodilation, congestion and production of heat locally as a result of the resistance of the tissue to the passage of the current undoubtedly contribute in some measure to the benefits reported from iontophoretic treatment with copper sulfate. Consideration must also be given to the suggestion of Szczerbak<sup>31</sup> that the galvanic current stimulates the sympathetic-parasympathetic system to produce reflex changes in the tissues treated by iontophoresis. These effects of the current on the tissue and on the copper sulfate solutions must be considered in evaluating the therapeutic benefits reported in the past in the treatment of diseased surface tissues with copper sulfate solutions by iontophoresis, since the penetration of copper

in the absence of detergents or organic salts of the metal to facilitate the introduction of copper into tissue has been shown in these experiments to be extremely limited

#### SUMMARY

1 Iontophoresis increases the electrodeposition of copper on the surface of the genital tissue of rabbits treated with aqueous copper sulfate solutions. It does not further the introduction of copper beyond the surface epithelium.

2 By adding aerosol MA to solutions of copper sulfate, the penetration of copper by iontophoresis was increased approximately twenty-five times.

3 Maximal penetration of copper was obtained with iontophoresis by incorporating the copper in an organic salt, bis(trimethylenediamino)cupric sulfate.

4 Solutions of copper and aerosol MA or the organic copper salt applied topically without iontophoresis do not produce penetration of copper.

5 Copper is prevented from penetrating surface tissues by the tissue proteins which combine with it. The addition of aerosol MA to solutions of copper sulfate inhibits this binding of copper by tissue proteins. The incorporation of copper in organic salts prevents this interaction of copper with tissue proteins.

6 The amounts of copper introduced into surface tissue treated by iontophoresis with aqueous solutions of copper sulfate and detergent or solutions of organic copper salt depends on the strength of current employed, the duration of treatment and the concentration of the salts used. Toxic effects of copper must be guarded against when using these preparations by iontophoresis.

30 Molitor, H., and Fernandez, L. Studies on Iontophoresis. I. Experimental Studies on the Causes and Prevention of Iontophoretic Burns, *Am J M Sc* **198** 778-785 (Dec) 1939.

31 Szczerbak, cited by Karbowski, M. Iontophoresis in Ophthalmology, *Internat J Ophth* **97** 166-202 (June) 1939.

# WHITE CROSS STRIAE OF THE FINGER NAILS FOLLOWING CARDIAC INFARCTION

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Changes in the finger nails of patients with cardiac disease are caused principally by congestion in the venous system. The bluish discoloration of the nails is a symptom well known to every physician. When the congestion persists for some time, the matrix bulges while the nail bed and nail wall manifest less conspicuous changes. The process results in the formation of "hippocratic" nails and of clubbed fingers.

According to Heller,<sup>1</sup> the eminent authority on diseases of the nail, all other changes in the nail in patients with cardiac involvement must be regarded as great rarities. Subungual keratosis is occasionally observed. Only in 1 case of myocarditis Heller observed broad transverse furrows (the so-called Beau lines). These transverse sulci had made their appearance seven and five months previously, at a time when the patient was suffering severe general manifestations notably high grade edema.

Endocarditis lenta is the one disease in which, as Pardo-Castello<sup>2</sup> has pointed out, vibices in the form of transverse lineal hemorrhages are observed as a constant phenomenon.

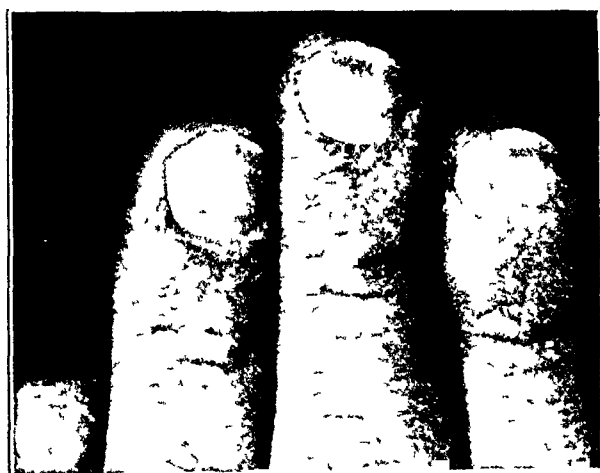
Even when the major peripheral vessels are occluded, this only rarely leads to changes in the nails. Heller<sup>1</sup> examined a great number of patients with thrombosis and embolism in the Berlin hospitals and encountered but 1 instance of gangrene in the toes (in a patient with embolism of the femoral artery). Furthermore, he cited Wilkin's case, in which the occlusion of the brachial artery through embolism caused the entire arm to be cold and pulseless. When the circulation was restored and the arm apparently became normal again, all the finger nails fell off. The disturbance in the blood supply was undoubtedly greatest in the distal ends of the extremities.

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1 Heller. *Die Krankheiten der Naegel, in Jadasohn, J. Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1927, vol 13, pt 2.

2 Pardo-Castello, V. *Diseases of the Nails*, ed 2, Springfield, Ill., Charles C Thomas, Publisher, 1941.

On the other hand, changes in the nails of the fingers and toes are commonly encountered in Raynaud's disease and in thromboangitis obliterans, in which the distal parts of the peripheral vascular system are chiefly affected. These changes run the whole gamut from cyanosis, to begin with, to the development of Beau's lines and, finally, to gangrene. Similar pictures are to be seen in cases of senile or diabetic gangrene of the extremities.



White cross striae of the finger nails appearing fifty-five days after cardiac infarction.

## REPORT OF A CASE

Dr K. S., a 50 year old physician, suffered typical attacks of the anginal syndrome in 1938 and 1939. After medication with glyceryl trinitrate and restriction of the patient's activities, the attacks ceased completely. The electrocardiogram revealed the presence of a right bundle branch block, which however did not bring on any clinical or subjective manifestations. Without any apparent cause, precordial pains began on Feb 12, 1944. These were followed, five days later, by an attack of intense pain and by shock. The blood pressure fell to 90 systolic and 60 diastolic, remained at that level for some ten days and then slowly rose to 110 systolic and 70 diastolic. During the first two days the temperature was 101 F, leukocytosis was present, and a gallop rhythm was heard. The patient lost about 10 pounds (4.5 Kg) during the first week of his illness. The electrocardiogram confirmed the diagnosis of myocardial infarction. The patient remained in bed for four weeks, then he made a relatively speedy recovery.

On April 8, fifty-five days after the appearance of the cardiac infarction, the patient noticed that the nails of all his fingers, with the exception of his thumbs,



showed transverse lines, about 2 mm in width, located at the boundary of the first and second quarters of the nails. The color of these lines was not really white but of the tint of the lunula of the nails. These streaks ran from one side of the nail to the other. The overlying surface of the nails showed no depression or other irregularity. When the hands were raised, there was no change in the width or intensity of the white lines, but when the fingers were allowed to hang down there was a decided whitening of the nails, which extended from the nail wall to the streaks previously mentioned, so that the lower third of the nails looked entirely white.

The lines grew forward continuously, those of the second and third fingers reached the free end of the nail eighty days after the appearance of the cardiac infarction, while it took the lines on the nails of the little finger ninety-four days and those of the fourth finger one hundred and ten days.

It is interesting to note that there was great symmetry in the progress of the lines on the fingers of both hands. The varying lengths of time required for the lines to disappear from the nails of the different fingers may probably be explained by the fact that the arterial blood supply to the extremities of the separate fingers was interrupted or impeded for different lengths of time. Lastly, it must be noted that the patient's finger nails were relatively small, their length ranging from 8 mm (on the little finger) to 11 mm (on the middle finger).

#### COMMENT

Heller stated that the white transverse lines are the equivalent of Beau's lines. Almost one hundred years ago, Beau<sup>3</sup> described sulci limited posteriorly by slightly elevated ridges that first appear at the lunula and progress forward with the growth of the nail until they disappear at the free edge. These so-called Beau lines are due, as Pardo-Castello<sup>2</sup> has explained, to a sudden arrest of the function of the matrix which, in turn, leads to the cessation of normal cell production, thus the continuity of the nail plate is broken. The principal underlying causes of the Beau lines are acute infectious diseases, diseases accompanied with fever, acute gastrointestinal disturbances and poisoning, as well as other serious conditions affecting the nutrition of the organism. On the other hand, Beau's lines have apparently never before been observed in connection with cardiac disease.

The literature contains relatively few descriptions of white cross striae (Vogel,<sup>4</sup> Wagstaffe<sup>5</sup> and Heller<sup>1</sup>). Heller expressed the opinion that they are produced in the following manner. At

the time of the general trophic disturbance the matrix forms nail cells which have an abnormal tendency to imbibe quantities of air. However, newer histologic investigations (Alkiewicz) suggest the probability that the white discoloration is caused by pathologically cornified nail cells.

The appearance of white cross striae on most nails about fifty-five days after the acute occlusion of one of the coronary vessels is an unfailing indication that the blood supply to the body's periphery was, for some few days at least, wholly inadequate. This view is also corroborated by the low blood pressure and the great loss in weight.

As far as I have been able to determine, neither the white cross striae nor the Beau lines have ever been mentioned in the literature on cardiac or vascular diseases. The question arises whether the disturbance in blood supply in cardiac infarction is in general not severe enough to cause these nail manifestations or whether they have merely escaped the physician's attention. It will be relatively easy to answer this question by systematically examining the nails in cases of coronary thrombosis, now so commonly encountered.

Assuming, as Heller<sup>1</sup> did, that the nails grow at the rate of 0.1 mm per day and that the average length of the covered part of the nail is from 3 to 4 mm, then a pathologic disturbance would become visible on the nail wall in from thirty to forty days. The white lines were about 2 to 3 mm from the nail wall when they were first observed by the patient, on the fifty-fifth day after his attack. This would lead to the conclusion that the growth of the nail itself was not affected.

Last, it should be stressed that the presenting nail disturbance is in no way to be regarded as a variant of leukonychia striata. In the latter disease the whiteness is much greater and lacks the lunula-like tint, moreover, leukonychia striata hardly ever appears as a single, isolated, relatively broad streak but rather as a number of parallel narrow lines, some of which do not run all the way across the nail but cover only a part of the width of the nail.

#### SUMMARY AND CONCLUSIONS

Disturbances of the nails that are associated with vascular and cardiac diseases are briefly considered.

In 1 case white cross striae of the nails, appearing fifty-five days after the onset of coronary occlusion, are regarded as an expression of a severe generalized nutritive disturbance resulting from damage to the cardiac muscle.

3 Beau, J. H. S. Certain caracteres de semeiologie retrospective, presentes par les ongles, *Arch. gen. de med.* 9:447, 1846.

4 Vogel, A. Die Naegel nach fieberhaften Krankheiten, *Deutsches Arch. f. klin. Med.* 7:333, 1870.

5 Wagstaffe, W. On Cross Furrows in the Nails, *St. Thomas Hosp. Rep.* 18:173, 1890.

## CLASSIFICATION OF TUBERCULOSIS OF THE SKIN

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Tuberculosis of the skin is so rare in the United States that the question may be asked why attention should again be drawn to its classification. The dermatologic manifestations of tuberculosis are extremely diverse and even though all are due to the tubercle bacillus it would be not only inadequate but a long step backward to call them all merely "tuberculosis of the skin." What then are the purposes of a classification? Obviously the most important one is to afford the physician an adequate basis for a correct prognosis for a given tuberculoderma as well as to aid in the proper management of the individual case. Because of the great variation in the severity, course and prognosis of the various forms of cutaneous tuberculous inflammation a more specific diagnosis than "tuberculosis of the skin" is essential. Furthermore, it is by means of classification that both undergraduate and postgraduate students of dermatology are taught cutaneous tuberculosis, and in the final analysis that classification is the most acceptable which best enables them to give a prognosis and to outline therapy in a certain case.

A critical review of the literature and our own clinical material over a long period brings realization of the constant but fluctuating struggle between the invading virus and the resisting forces of the host and permits understanding of the phases of activity and quiescence of the disease. Thus the characteristics of a certain tuberculoderma may vary considerably from time to time, despite the fact that the host, although altered allergically, is the same and the invading organism is the same tubercle bacillus throughout the course of the disease. Such a concept permits realization of the difficulties in forming arbitrary classifications with sharply drawn distinctions between the various tuberculodermas.

As knowledge of tuberculosis of the skin evolved, early writers described various types without considering the relation of one to another. Observation soon showed, however, that patients

often had more than one form of tuberculosis at the same time. Such associated conditions as lupus vulgaris and scrofuloderma, tuberculous adenitis and lichen scrofulosorum and mucosal tuberculosis and severe or terminal pulmonary, intestinal or urogenital tuberculosis were frequently seen. These associations naturally stimulated interest in their relations and through the years constant effort has been made to find a cornerstone on which to build a suitable classification.

At one time much attention was paid to the species of bacillus, and this still may be more important than one realizes. With a basis for classification in mind students of tuberculosis in the early nineteenth century were greatly concerned as to whether a cutaneous lesion was of external or of internal origin and whether the bacillus was exogenous or endogenous.

The growth, development and dissemination of tuberculous lesions of the skin have been and still are the subject of much conjecture. Many years ago writers called attention to the characteristics of certain lesions which from their strictly localized nature were assumed to be caused by the implantation of bacilli, either externally or lymphogenously at a certain site. Later when the concept of tuberculids was advanced attention was focused on the hematogenous dissemination of the causative agent and various tuberculodermas were arbitrarily grouped together as forms of hematogenous tuberculosis.

Authors of most present day classifications of tuberculosis of the skin have considered the following points stressing one or another as being most important: (1) mode of arrival of the bacillus at the site of the cutaneous lesion, (2) clinical features, (3) histologic and bacteriologic features, (4) immunologic status and (5) prognosis.

In our opinion, it is presumptuous to base a classification on the mode of arrival of the bacillus at the site of the tuberculous lesions. Lupus vulgaris has been classified as a localized form of cutaneous tuberculosis yet for patients who have multiple, widely disseminated but morphologically characteristic lesions associated with internal tuberculosis a hematogenous dissemination seems to be the only tenable explanation. Therefore,

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lupus vulgaris can hardly be classified as a strictly localized form of tuberculosis. The same statement is true of colliquative tuberculosis, especially those forms known as tuberculous gummas or those which extend from tuberculous bones.

Studies on pulmonary tuberculosis have shown that bacilli may be and often are hematogenously spread even in cases of pulmonary tuberculosis, in which, for example, there is infection of the lung secondary to intestinal tuberculosis. If bacilli can have their entrance in the intestinal tract and eventually reach the lung, they must also reach the skin, where in some instances they

portant information, since it is impossible even to begin a classification unless the various tuberculodermas can be correctly recognized and given specific names. On the other hand, the clinical features alone do not always afford sufficient evidence for the final labeling of a tuberculoderma. A single nodule of lupus may be indistinguishable from a single nodule of tuberculosis miliaris disseminata faciei, and the small papular forms of sarcoid were often called lupoid because it was impossible to differentiate them morphologically. All in all, however, the clinical features of tuberculodermas are consistent, and from a practical standpoint this is extremely important.

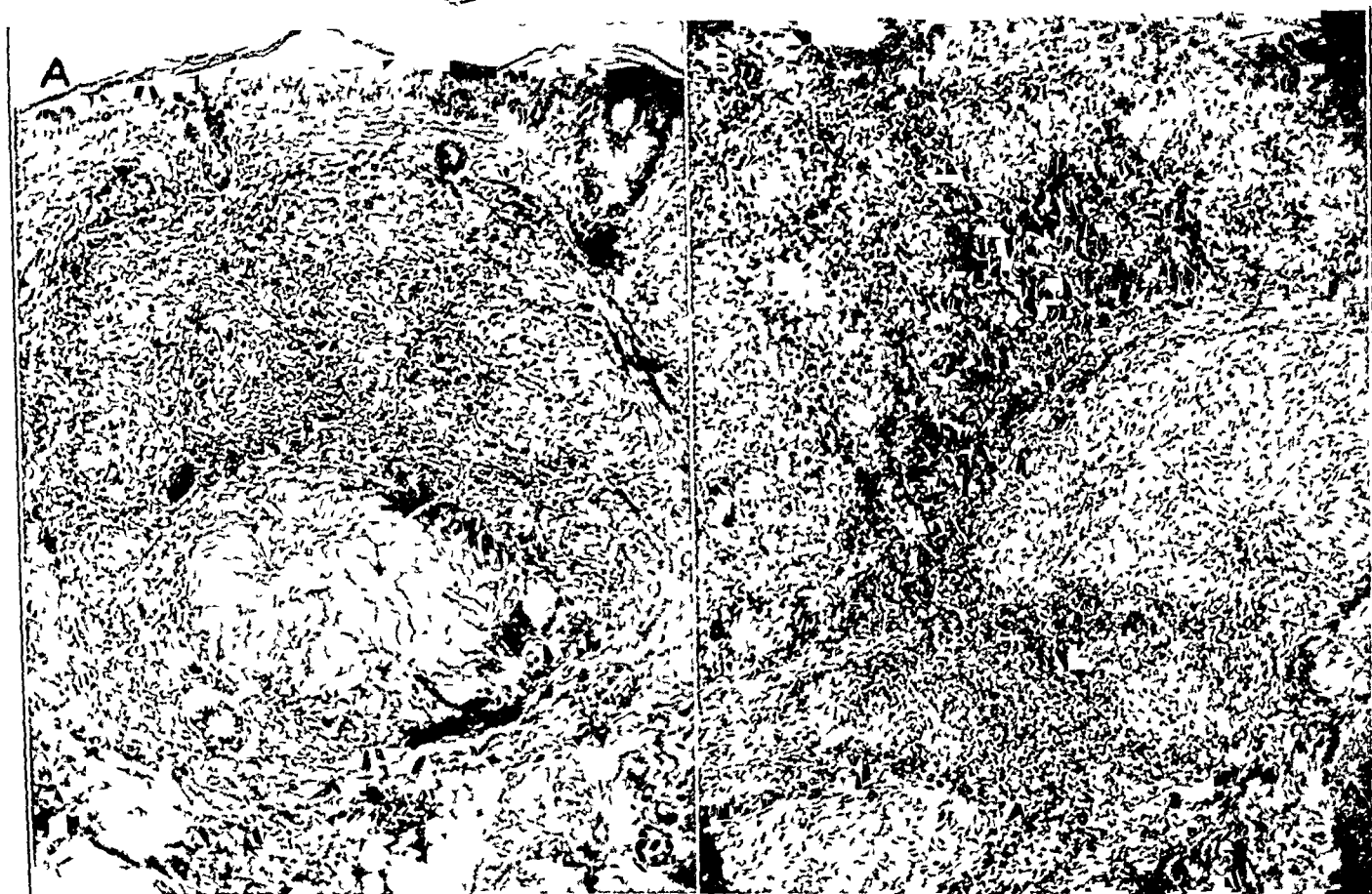


Fig 1—Sections from a case of lupus vulgaris showing (A) the rare feature of caseation necrosis and (B) changes simulating those of sarcoid.

lie dormant as saprophytes, eventually being destroyed, and in other instances they produce lesions. Strictly speaking, the lesions are of hematogenous origin, although from a practical standpoint their growth is local. Many possibilities can be hypothesized, but we are convinced that, since it is utterly impossible to know definitely how the bacillus reaches its site of growth, such a premise is an inexact basis for a classification. Moreover, to know how the bacillus reaches the site of future disease is not as important as to know what develops after it arrives there.

The morphologic features of the various forms of cutaneous tuberculosis afford the most im-

portant information. The onset of a tuberculoderma is important. For example, lupus vulgaris begins insidiously with one or a few lesions in one locality. The patient can hardly state when the disease began. Tuberculids, on the other hand, begin explosively with the sudden appearance of disseminated lesions, which are often grouped. This is significant because very likely when a patient is a candidate for lupus vulgaris his tissues possess certain qualities in relation to tuberculosis which predispose to that form of reaction. Although we do not know what these qualities are, they must be those on which an accurate classification could be based. Therefore, tuberculosis of the skin may be divided into two main groups (1) the

stable forms, as exemplified by lupus vulgaris, and (2) the labile, or transient, forms, typified by the tuberculids

The age of the patient apparently has something to do with his susceptibility to certain forms of cutaneous tuberculosis. For example, the rare postexanthematic miliary tuberculosis occurs only in children. Tuberculosis lichenoides (lichen scrofulosus) is never seen after the second decade. Lupus vulgaris in the majority of instances has an early onset, even though it may begin in advanced years, and Jadassohn brought out that a peculiar fungating form of colliquative tuberculosis is much more common in aged persons than in children.

At one time it was believed that the histopathologic features of the various forms of cutaneous tuberculosis were pathognomonic. In the main, they are extremely helpful in the diagnosis of tuberculodermas, but more complete studies, especially with multiple sections, have proved that almost any form of tubercloid structure can be found in almost any tuberculoderma. For example, tuberculosis miliaris disseminata faciei has been described and accepted as a form of tuberculosis which always shows a sharply circumscribed tuberculoma with central caseation. Nevertheless, we have observed cases in which the diagnosis was clinically beyond question and yet these features of the disease were not encountered. Lupus vulgaris is said to show little if any caseation necrosis, nevertheless we have seen this feature repeatedly in sections from cases which were clinically unmistakable. Similarly, in our studies of the micropapular tuberculid we found sections which were indistinguishable from cutaneous sarcoids. Even in the two main forms of cutaneous tuberculosis, the stable and the labile, histologic differentiation is sometimes impossible, since lupus vulgaris can mimic almost every other type of tuberculosis of the skin. We do not believe that histologic methods of any kind give definite information as to how the tubercle bacilli arrive at the particular area of the skin which is to be the site of future disease.

It must be emphasized that the microscopic anatomy of a given lesion varies greatly with its age as well as with other intrinsic and extrinsic factors. It may be necessary to perform a number of biopsies before a diagnosis can be made. It is also most important that more than one section be examined microscopically and that whenever possible serial, or at least multiple, sections be made.

Since various tuberculodermas are often strikingly similar, it is impossible to draw sharp lines

based on histopathologic observations which would definitely separate one type of tuberculosis of the skin from another. Histologic differentiations are based on the preponderance of lymphocytes, epithelioid and giant cells and necrosis. The depth of the infiltrate, the dimensions of the inflammatory zone and its relation to blood vessels and the secondary epidermal changes are other features to be considered. The value of histopathologic examination is greatly increased if the dermatologist who has examined a given tuberculoderma clinically can also study the sections. An independent microscopic examination may be confusing and in some cases inaccurate.

It should be mentioned that long before the histologic changes can be determined as characteristic, the pattern for a particular patient has been laid down by his own physiologic reactivities. It takes some time, however, for the pathologic elements to come more or less into equilibrium with their surroundings, hence variants seen for the same morphologic type. If the histologic sections of various forms of tuberculosis of the skin are compared, remnants of blood vessels are seen within the infiltrate of all. In erythema induratum this is especially striking, in the necrotic papular tuberculid the vessel remnants are in the cutis, but in lupus vulgaris, if the specimens for biopsy are cut deeply enough, involvement is found in all the layers of the skin and the vessels of the cutis and subcutis seem to be at the center of the masses of infiltrate. If tissue adjacent to blood vessels is examined, strands of infiltrate will be found, especially near veins.

From this it may be deduced that almost all forms of cutaneous tuberculosis have their origin in or about vessels. Their size and depth must play an important role in the appearance of the resulting lesion, and these, together with the different forms of epidermal response and different degrees of necrosis, help determine the morphologic appearance.

Bacteriologic observations, except for an extremely few types of cutaneous tuberculosis, are not a great help in forming a classification. Bacilli may be easily found only in primary cutaneous tuberculosis, the ulcerating orificial type and generalized miliary tuberculosis of the skin. In some cases of other types, bacilli can be found only if the search is undertaken at a particular time in the life cycle of the lesion. Culture of bacilli and animal inoculations, as far as tuberculosis of the skin is concerned, are too tedious and painstaking to be practical. It would be highly desirable to find bacilli in every case of cutaneous tuberculosis, and it is to be hoped that simpler and more ac-

curate methods for finding them in cutaneous tuberculous inflammations will be developed

Ascertaining the degree of allergy, as revealed by the patient's reaction to tuberculin is essential in completing the study of a patient with tuberculosis of the skin. This determination alone, however, is not an accurate basis for classification, because the degree of sensitivity does not depend on the cutaneous lesion alone. In fact, the cutaneous lesion may have nothing to do with sensitivity to tuberculin in a particular patient, and if one adheres to the assumption that almost all cutaneous tuberculosis comes from an internal focus one must admit that sensitivity to tuberculin results from the reaction against this internal infection. If hematogenous cutaneous tuberculosis is accepted as a large group classification, an internal focus must be admitted, and therefore it may not be stated that certain forms of hematogenous cutaneous tuberculosis consistently have specific degrees of tuberculin sensitivity, for obviously the internal focus must be the source of the bacilli and also the provocator of the state of allergy. Knowledge of the reactivity to tuberculin in a certain case does not help to any great extent in diagnosing the case clinically, because reactivity to tuberculin is not consistent enough in like forms of cutaneous tuberculosis. The degree of sensitivity would be a convenient basis for classifying tuberculodermas, but, unfortunately, it does not stand critical analysis.

If an attempt were made to classify a large group of patients in a sanatorium entirely on their sensitivity to tuberculin, a great variance between the state of allergy and the clinical and roentgenologic observations would undoubtedly be found. Both of the latter are much more valuable than sensitivity in predicting the future course of the disease, and discrepancies in the reaction to tuberculin would not alter the clinician's appraisal of the case. Similarly, the clinical and histologic observations in cutaneous tuberculosis cannot be ignored because the sensitivity to tuberculin does not happen to be what was expected.

Thus, we come again to one of the important purposes of classification, which is to enable the physician to make a prognosis. The prognosis of a certain tuberculoderma, of course, depends on the general resistance of the host, but experience has shown that in most cases of a particular form of cutaneous tuberculosis there is close similarity in the outlook. On the basis of prognosis certain tuberculodermas may be grouped together, and if those which are placed in the same

group are critically analyzed common characteristics can be found which assist in classification.

On the basis of prognosis, therefore, we offer the following classification of cutaneous tuberculosis

- A Forms which are chronic and progressive, rarely terminating fatally
  - I Tuberculosis cutis luposa
  - II Tuberculosis in the American Negro (cause debatable)
  - III Sarcoidosis (cause debatable)
- B Forms which tend to heal
  - I Relatively rapidly
    - a Primary cutaneous tuberculous complex
    - b Tuberculosis cutis verrucosa
    - c Tuberculosis cutis lichenoides (lichenoid papular tuberculid)
    - d Tuberculosis cutis papulonecrotica (necrotic papular tuberculid)
  - II More slowly
    - a Tuberculosis colliquativa (scrofuloderma)
    - b Erythema induratum (necrotic nodular tuberculid)
    - c Tuberculosis miliaris disseminata faciei (lupoid papular tuberculid)
- C Forms which usually terminate fatally
  - I Tuberculosis cutis miliaris acuta generalisata
  - II Tuberculosis cutis orificialis

The first group includes lupus vulgaris and cutaneous sarcoid (if it is tuberculous). Here a high degree of immunity is found, but the resistance is not great enough to overcome the disease, and lupus vulgaris therefore persists for years. Nevertheless, death from pulmonary tuberculosis in patients with lupus is not a rare occurrence, and there seems to be a relation between the cure of the external lupus and the unsatisfactory progress of the internal lesions so much so that it is impossible to think of lupus vulgaris as being merely an external disease.

The cutaneous primary complex, tuberculosis cutis verrucosa, and the necrotic papular and lichenoid tuberculids have in common the tendency to heal spontaneously. They vary greatly in their appearance and in their histologic structure, but they maintain a reasonable uniformity in sensitivity to tuberculin. We believe that patients with tuberculodermas in this group must possess a similar degree of immunity and hence must have a similar prognosis.

Erythema induratum and colliquative tuberculosis also tend to heal, even though it takes a long time. The degree of immunity in patients with these diseases is high, but it is not maintained at a fixed level, as manifested by numerous recurrences. Not only does the immunity change in patients with tuberculosis of the skin but the degree of allergy changes. This is best demonstrated by the rather short period in which a primary cutaneous lesion maintains its original char-

acteristics and also by its frequent metamorphosis into lupus vulgaris

Acute miliary cutaneous tuberculosis and ulcerating mucosal tuberculosis have much in common. The degree of immunity is extremely low. The bacilli grow unchecked, and the patients often die of tuberculosis, although one expects a negative reaction to tuberculin, a positive reaction may be found in the ulcerating mucosal form. Even though these two types behave alike in many ways, the histologic changes are different. However, acute miliary cutaneous tuberculosis and the ulcerating mucosal type must be thought of as closely related in most of their characteristics.

In tuberculosis of the skin, even though various appropriate names are evolved, it may be readily understood that there is a close similarity and relationship between types. Figure 2 shows the

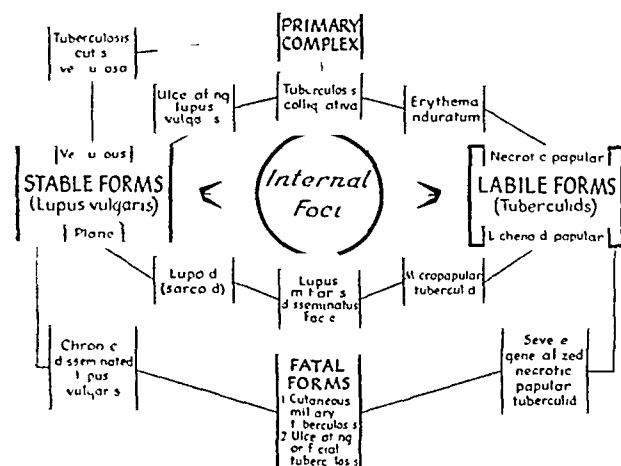


Fig 2—Relations of important forms of cutaneous tuberculosis

two basic forms—the stable, or long lived, as exemplified by lupus vulgaris, and the labile, or shorter lived, as exemplified by the tuberculids with their various ramifications merging into one another.

#### SUMMARY

Tuberculosis of the skin should be classified into its various types in order to expedite treatment and the formulation of an accurate prognosis. The clinical features give the most important information in forming such a classification.

The mode of arrival of the bacilli at the site of future disease and the morphologic, histologic, bacteriologic and immunologic features of a particular type of cutaneous tuberculosis are factors which must also be considered in forming a classification.

Grouping tuberculodermas according to the prognosis affords a simple and practical means of classification.

#### ABSTRACT OF DISCUSSION

DR. RUBEN NOWLAND, Iowa City. The physician who sees relatively few patients with cutaneous tuberculosis needs a great deal of help, and it seems that the textbooks in their classifications, whether by immunologic principles or by method of arrival of the bacillus at the source of infection, have not given us particularly helpful information. The microscopic characteristics of tuberculosis cannot determine a classification because of their great variation in various stages of any given eruption. The clinical features of cutaneous tuberculosis, as Dr. Michelson pointed out, are still the criteria that will guide us in making a diagnosis. Because the prognosis is so much more important than the diagnosis, I think that the present classification will prove a good thing and help those who see relatively few patients with cutaneous tuberculosis.

DR. FRED D. WEIDMAN, Philadelphia. I have been charmed at the concise way in which this paper has been presented, including particularly the diagram. I must say, though, that I disagree with the authors on one technical matter. If this paper were entitled "Some Remarks on the Clinical Classification of Tuberculosis" the title would be more accurate, my point being that there is no such thing as one, and only one, system of classification for anything, whether it is disease or botanic or zoologic forms. Any one has the right to arrange data to suit his particular needs. Thus, in mycology let the botanists employ, if they will, Saccardo's classification, which is based on the color of the fungi, but physicians prefer to use Castellani's medical classification of fungi or a simplified classification which depends on the forms that the fungi take in the tissues. A histologic classification is entirely in order for tuberculosis of the skin, and some day it may become useful to arrange a bacteriologic one. The one presented today is a clinical one, with the clinical forms as the criteria.

I was particularly pleased because the matter of degeneration of blood vessels was brought into the discussion. I have been impressed with this phenomenon, particularly in cases of erythema induratum, and many times this involvement of the vessels has made me pause to consider whether I am dealing with some disease more highly toxic than tuberculosis, such as rheumatism. I believe that the form which the necrosis takes in erythema induratum is largely a reaction against the necrotic fat that is more or less accidentally located at the site of this deep tuberculid process. The destruction of this fat causes the liberation of various lipid substances, and after that a conspicuous foreign body type of granulomatous reaction that may quite overshadow the genuine tuberculous reactions. I believe that a great deal of the reason for the use of the term "tuberculoid" in describing the reaction in erythema induratum is due to this necrotic process and not to the activity of the tubercle bacillus itself. I have seen classic tubercles well out in the periphery of the lesion, whereas in the more central, fatty parts the reaction was that which most histologists emphasize and which they call "tuberculoid."

DR. HAMILTON MONTGOMERY, Rochester, Minn. Dr. Michelson and I were agreed on the major point, although we may differ as to the importance of certain pathologic classifications. As Dr. Weidman said, any one can have his own classification and yet recognize the disease and treat and care for the patient in the same way as some one else.

In studying a given case of cutaneous tuberculosis one should not depend on the clinical appearance alone or on the other hand on a single laboratory report.



whether it is a histologic study, tuberculin reactions, roentgenologic findings or inoculation of guinea pigs. It is important to correlate all data in any given type of cutaneous tuberculosis.

Dr Laymon illustrated a case of lupus vulgaris in which the histologic structure in one area resembled that of sarcoid and in other areas revealed considerable caseation necrosis and simulated closely the histologic characteristics of scrofuloderma. I have also seen such structures. The pathologic criteria which I laid down some years ago (*Histopathology of Various Types of Cutaneous Tuberculosis*, *ARCH DERMAT & SYPH* 35:698 [April] 1937) took cognizance of the fact that lupus vulgaris does not run true to form in all cases. In a recent study of erythema induratum and allied conditions with Dr O'Leary and Dr Barker, we found that of some 72 cases which were classified as cases of erythema induratum on the basis of clinical and laboratory studies, only 70 per cent showed specific tubercle formation. In the other 30 per cent there were no classic tubercles, with central caseation and zones of epithelioid and giant cells and lymphocytes. Rather, there was a tuberculoid structure with irregular collections of giant cells, including foreign body giant cells and epithelioid cells, but without the regular pattern of a definite tubercle. Repeated specimens for biopsy in 1 case failed to establish the diagnosis of tuberculous erythema induratum, which was finally proved with the inoculation of a guinea pig. The classification which Drs Michelson and Laymon have presented is a clinical one, directed toward prognosis and treatment, and with which, from this standpoint, I am in entire accord.

Dr A ROSTENBERG, Washington, D C. As I understand the paper, the authors think that the best method of classification is to consider the clinical characteristics and to label the tuberculoderma according to these characteristics and then to prophesy the ultimate course of the dermatosis from that label. It seems to me that this is somewhat fallacious. After all, what determines the clinical characteristics of any tuberculoderma or, for that matter, any entity? It is the response of the body as a whole to the causal agent, which in this case is the tubercle bacillus.

The same thing that determines the particular appearance of the tuberculoderma for any patient determines the prognosis and is in a sense really the immunologic aspect of that patient.

If by the use of the term "immunologic aspect of the tuberculodermas" the authors mean only the tuberculin test, I can quarrel with them. Naturally, just from the injection of a small amount of tuberculin into the skin and the reading of that reaction twenty-four to forty-eight hours later one is not in a position to classify a dermatosis and to predict what will happen one week or one year or ten years from the time the test is made. But that is only one small fact in the whole immunologic picture. The whole immunologic picture, the dermatosis seen at the time of examination, the reaction to tuberculin and the prognostic implications are all interrelated. Therefore, it would seem to me that we are not advancing our thinking unless we view these factors as dynamic processes, and in that respect I think that many of you will recall an article written several years ago by the late Dr Moses Scholtz, which was called "The Dynamics of Cutaneous Morphology" (*ARCH DERMAT & SYPH* 33:605 [April] 1936). I think that is the point of view that must be taken with regard to such processes.

Dr ROBERT BRANDT, Cincinnati. A few years ago complement fixation tests were performed on patients with tuberculosis of the skin. From the results obtained, helpful hints might be derived for classification. There was a striking difference in the frequency of positive reactions among patients with different types of dermatologic tuberculosis, ranging from almost 100 per cent for patients with papulonecrotic tubercles to 30 per cent for patients with lupus vulgaris and none at all for patients with glandular tuberculosis. The percentage in cases of erythema induratum, of rosacea-like tubercle and of similar diseases was between 80 and 30 per cent. One may assume that fundamental biologic differences are mirrored in these wide variations of serologic reactivity. In accordance with Dr Montgomery's declaration that the whole immunologic aspect rather than only one test should decide the classification of tuberculous cutaneous manifestations, I think that serologic reactions should prove especially valuable.

Dr HENRY E MICHELSON, Minneapolis. Dr Nomland states that he sees so few cases of tuberculosis of the skin that he feels that we all need help in dealing with the problem. I quite agree with him, because none of us see enough of this condition to feel entirely certain about the findings. That is the very reason that we have been trying to get a classification that pleases us, so that when a case is encountered we will be able to place it in a general group and then study the details later, for more accurate knowledge.

Dr Weidman asked the reason for basing our classification on the clinical approach. We feel that that was the only approach which was at our disposal, for if we made a conclusion based on anatomic location errors would be very frequent, for example, not every tuberculous lesion on the face is rosacea-like tubercle and not every tuberculous lesion on the leg is erythema induratum.

Dr Weidman is correct in that the tuberculoid structure in erythema induratum, for example, is a reaction against fat necrosis, however, this is not due to injury of the fat but to inflammation. We have used the term "fat replacement infiltrate" in describing the changes that take place in erythema induratum.

Dr Laymon and I have discussed the use of the word "hematogenous" as used by Gans, and we feel that one should not use this term in relation to tuberculosis of the skin, because one does not know that the bacilli arrive at a certain spot by way of the blood stream. We have been more willing to use the term disseminated and localized rather than hematogenous and localized.

Dr Rostenberg objected to our making our classification on the basis of clinical observation. We have been more concerned with the way in which the patient combats the disease than with a discussion of his sensitivity to tuberculin, because sensitivity is not, in many cases, an indicator of the resistance of the patient. Many times we have seen forms of cutaneous tuberculosis in which, on the basis of the lesion and the patient's sensitivity to tuberculin, one would state that the prognosis was good, but after observing the patient over a period, we have seen fatal results where least expected. This is a matter of resistance, and to me it is important.

We proposed this mode of approach, and we feel that it is based more on logical conclusions than on so variable a thing as sensitivity to tuberculin, and we furthermore believe that the morphologic characteristics and the clinical course are important.



## EXTRAGENITAL SYPHILITIC INFECTION IN NEGROES

H. H. HAZEN, M.D.

WASHINGTON, D. C.

Since my connection with the Howard University College of Medicine, that is, during thirty-three years, I have made a record of every Negro patient observed with dermatologic disease or syphilis.

One of the most striking observations of this study has been the paucity of early syphilitic infection with extragenital chancres. All told, there have been seen 600 patients with chancres and 3,100 with early secondary lesions, each of the latter was investigated for the site of the initial lesion. Only 19 extragenital chancres were found. Of these, 12 were situated on the lips, 2 on the tonsils, 1 on the tongue, 1 on the breast, 1 on the finger and 2 in the groin. In addition, there was 1 on the base of the penis, which can hardly be classified as extragenital. This gives the percentage of extragenital chancres in this series of Negroes as 0.51. Two other patients with extragenital, exclusive of congenital, infections were seen. One was a patient with transfusion syphilis, and the other was a young surgeon who was inoculated through a slight cut of the hand while operating on a patient with acute secondary syphilis. There was no initial lesion.

A comparison of these values with the values for extragenital infections in white persons seems necessary for two reasons. First, many syphilologists are ignorant as to the number of these infections, and, second, the seriousness of extragenital infection is not appreciated in many quarters, especially religious ones, which still hold that syphilis is a result of moral lapse.

Solomon and Solomon<sup>1</sup> devoted several pages to this subject. These authors gave a fairly complete bibliography of articles relating to extragenital chancres up to the date of publication, including the statistics of Bulkley, Porter, Montgomery, Pusey, Nichols, C. Morton Smith, Schour and Vedder. A study of these statistics reveals the probability that extragenital chancres constituted at least 5.5 per cent of the total number of extragenital infections.

Hazen<sup>2</sup> has reported the studies of Fournier, Cole and Schamberg, which yielded about the

same results. Kampmeier<sup>3</sup> gave the latest report, stating that in the Vanderbilt University Hospital Clinic the percentage of extragenital chancres was 5.5 per cent.

Even though it is admitted that extragenital infections are greatly decreased because of the present absence of (1) vaccination chancres, (2) eustachian tube catheterization chancres, (3) wet nursing chancres and (4) circumcision chancres, the fact still remains that approximately 5 to 5.5 per cent of all infections, exclusive of congenital ones, are extragenital.

Should one desire to pursue the question of innocent infections still further, it may be remarked that the percentage of congenital infections in Negroes is 3.6 per cent, as compared with 5.2 per cent in white persons.<sup>4</sup> It must be noted that this is the percentage of actual cases of syphilis discovered and does not relate to the total number of cases in the races. It should also be remarked that in the white race at least 20 per cent of syphilitic women are infected by their husbands.<sup>5</sup> How many men are infected by syphilitic wives is not yet determined—possibly 1 per cent.

It is obvious that 25 per cent of all syphilitic white women are infected through no fault of their own. It seems certain that at least 6 per cent of the infections in white men are innocent. When one adds the number of instances of congenital syphilis, even though one admits that they are on the decrease, exclusively because of good public health teaching and practice, it is certain that some 10 per cent of all infections in the white race are not due to illicit sexual intercourse. Unfortunately, there are no figures to show the number of innocent infections in the Negro race, with the exception of extragenital and congenital ones, which add up to a trifle over 4 per cent.

1911 R Street Northwest.

2 Hazen, H. H. *Syphilis*, ed. 2, St. Louis, C. V. Mosby Company, 1928, p. 78.

3 Kampmeier, R. H. *Essentials of Syphilology*, Philadelphia, J. B. Lippincott Company, 1943, p. 114.

4 Wenger, O. C. *Chicago Syphilis Control Program, in Annual Report United States Public Health Service*, July 1, 1940—June 30, 1941.

5 Fournier, A. *Treatment and Prophylaxis of Syphilis*, New York, Rebman Company, 1906, p. 36.

Hazen, H. H. Unpublished data.

1 Solomon, H. C. and Solomon, M. H. *Syphilis of the Innocent*. United States Interdepartmental Social Hygiene Board, Washington, D. C. 1922, pp. 188-195.

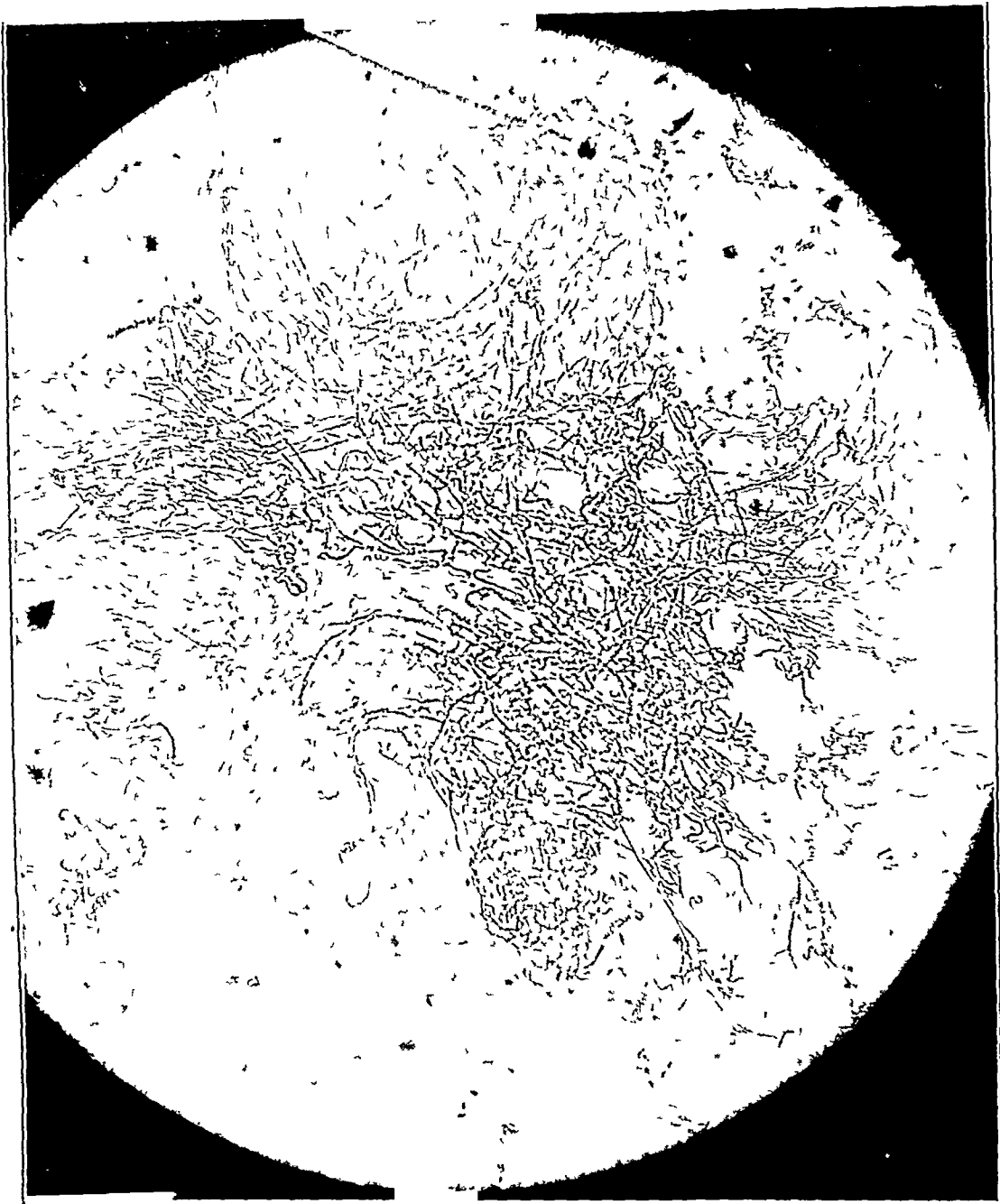
## Clinical Notes

### SEMBLANCE OF ELASTIC TISSUE TO MYCELIUM IN POTASSIUM HYDROXIDE PREPARATIONS

WALTER S GREEN, M D, and MAURICE C SHEPARD, M S  
GREENWOOD, MISS

The novice in the field of medical mycology may be readily deceived by potassium hydroxide preparations of shavings of skin which extend down into the corium

mycelium of fine, nonseptate, intertwining and branching hyphae. Although elastic tissue fibers are known to vary in thickness from a fraction of a micron to as



Photomicrograph ( $\times 100$ ) showing elastic tissue fibers in normal skin as prepared by digestion with 5 per cent potassium hydroxide solution and heat. Minute shaving was made parallel to the surface of the skin and extended down into the upper part of the corium.

Such specimens contain elastic tissue fibers which withstand digestion by potassium hydroxide and heat. The usual types of specimens examined in dermatologic practice, such as scales, scrapings and peelings of epidermis alone, naturally do not contain elastic tissue.

Under low power, high dry or oil immersion magnification, the elastic tissue fibers appear to be a dense

much as 11 microns in diameter, they appear deceptively uniform in potassium hydroxide wet mounts. The fluorescence of the elastic tissue fibers under ultraviolet radiation may serve further to confuse the observer. Nothing resembling spores is present.

Dr George M Lewis and Miss Mary E Hopper enlightened us as to the identity of this artefact.

## RINGWORM OF THE EYEBROW

EMANUEL MUSKATBLIT M D, AND NATHAN A TARGAN, M D, NEW YORK

Cases of ringworm of the eyebrow are rare and are worth reporting. A white boy, aged 9 years, presented what looked like a patch of tinea circinata over the left eyebrow. The lesion was annular, about 3 cm in diameter, with a slightly raised erythematous and scaly border and a center of almost normal skin. The hairs of the eyebrow seemed normal under ordinary light. Under Wood light however, many of them showed yellowish-greenish fluorescence along their entire length. In addition, there were several erythematous and scaly lesions on the left nuchal area and a large focus on the left occipital area of the scalp, all with long fluorescent

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Third Medical Division (New York University), Bellevue Hospital, service of Dr Frank C Combes

hairs. The patch on the scalp was visible only under Wood light and was unnoticeable under ordinary light, because there was neither erythema nor scaling and the hairs were not broken off short. Microscopic examination of hairs from the eyebrow and from the scalp revealed a microsporon, and the cultures from both produced *Microsporon audouinii*.

This case demonstrates the importance of the examination by means of filtered ultraviolet rays, which show involvement of hairs by microsporon when ordinary light fails to reveal any changes of the hairs or of the skin itself. It is also suggested that during examination for ringworm Wood light should be directed not only toward the patient's scalp but toward the face. If this is done systematically, it is possible that the incidence of ringworm of the eyebrows will be found to be higher than it is believed to be at the present time.

## Correspondence

### ONE HUNDREDTH ANNIVERSARY OF THE FIRST AMERICAN TEXT- BOOK OF DERMATOLOGY

*To the Editor*—American dermatologists should pause for a moment during the present mad rush of events to pay tribute to the memory of Dr Noah Worcester, formerly of Cleveland and Cincinnati, on the one hundredth anniversary of the publication of his book, which was the first American textbook of dermatology

Worcester's excellent book, "A Synopsis of the Symptoms, Diagnosis and Treatment of the More Common and Important Skin Diseases," was published in 1845, having been printed in Cincinnati by Shepard and Company for Thomas Cowperthwait and Company, of Philadelphia

Pusey in his "History of Dermatology" said that "Noah Worcester (1812-47) was evidently a man of unusual ability. Although he had to work his way, he was an A B of Harvard (1832), an M D of Dartmouth (1838) and in 1841 he went to Paris where he studied at St Louis Hospital for about eight months. He also studied in London and elsewhere in Europe for two or more years. He was a pupil of Laennec and was regarded by his contemporaries in Cincinnati and Cleveland as a leader in pathology and 'the best trained man in percussion and auscultation in America.' His untimely death from pulmonary tuberculosis in 1847 was regarded as a great loss." Pusey said further that Dr Worcester, at the time that the book was published, was professor of physical diagnosis and general pathology of the Medical School of Cleveland, though previously he had served as a professor in the Medical College of Ohio

Relative to Worcester's book on dermatology he said that "it is a large octavo volume containing 292 pages of text. The sixty colored illustrations are quite as good as those in contemporary European publications and must have been of European make. He acknowledges his indebtedness to the European masters from Willan and Wilson to Rayer and Gibert, but his work shows firsthand knowledge of dermatology. It is about the size of Bulkley's American edition of Cazenave's *Manual* (1852) and it does not suffer by comparison with it. His descriptions are clear, show familiarity with the subject and a temperate and scientific spirit. Although published in Philadelphia, it probably did not attract attention because the older states were hardly prepared to expect a useful book on dermatology to come out of a western outpost like Cleveland."

Dr Worcester brought with him to the then frontier state of Ohio the teachings of Harvard, Dartmouth and the best of Europe's great clinics and teachers. Unfortunately, a picture of him could not be found after a diligent search.

Reading through Worcester's book, one is made aware that, while many aspects of his writing are of another time, dermatology as it is known today was then having its beginning. The bacteriologic aspects of cutaneous disease were unknown, but fungi are given as the cause of favus, and the acarus of scabies is

described and is well illustrated, as is Demodex folliculorum. His descriptions of cutaneous lesions are clear and concise. The suggestions for therapy have a modern turn but with a definite leaning to purges, leeching and tonics.

However, he chided some of his contemporaries as the following quotation shows: "frequently no attempt is made to adapt the treatment to the character or stage of the disease, and consequently we ought not to wonder at the result, it is often directed by a physician incapable of giving the pathology of a single eruption, whose whole vocabulary of cutaneous diseases is confined to some four or five vulgar unmeaning names, as 'Salt Rheum,' 'Tetter,' and possibly 'Herpetic Eruption,' whose whole medical ammunition for their cure consists of some half dozen remedies, administered externally and internally according to some whim or fancied specific power, as Cream of Tartar, Sarsaparilla, internally to 'purify the blood,' Arsenic, Sulphur, Corrosive Sublimate prescribed internally as 'alterants,' and externally as 'stimulants,' and some irritating substances made into washes, or still worse, mixed with more irritating rancid lard, under the form of salves and ointments, intended to be applied externally 'to dry up the humor'."

"The great reason that the treatment of cutaneous diseases has generally been attended with so little success, is that we prescribe for them too empirically, and do not pay sufficient attention either to the pathology or to the stage of the eruption."

I believe that the readers of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY will find the book interesting and through it will be able to go back a hundred years to the dermatologic problems of that time. The book may be borrowed from the Library of the Surgeon General of the Army, Washington, D C. It is copy no 107017.

Thus, the year 1945 marks another anniversary in American medicine. We who are interested in dermatology are especially proud of the excellent textbooks on dermatology that have come from the United States during the last one hundred years.

Dr Noah Worcester's work recalls from the past the pioneering work of men such as he and gives to this generation of dermatologists inspiration and a challenge.

JAMES QUINCY GANT JR, M D, Bethesda, Md

### VITAMIN B COMPLEX FOR VITILIGO

*To the Editor*—About four years ago I prescribed vitamin B complex capsules, fortified with nicotinic acid, thiamine hydrochloride and riboflavin, and hydrochloric acid for 2 patients with mild pellagrous dermatitis. Both of these patients also had a long-standing vitiligo. Since this medication made them feel so much better, they continued taking the preparations. Over a year later these patients consulted me for unrelated conditions and during the consultation mentioned casually that their vitiligo had entirely cleared.

I therefore decided to try this therapy in other cases. Up to the present time I have had 14 patients report results. Seven of these reported that their eruptions had cleared entirely, and 2, that there has been decided

improvement All these patients were given 2 capsules of fortified vitamin B complex and 10 minims (0.6 cc) of dilute hydrochloric acid after meals All took the medication from one to two years and continued it in half the dosage after their eruptions cleared Of the other 5 patients who reported, 3 took the medication only at intervals, as they would often forget Any improvement in these patients was doubtful One patient discontinued the treatment because he developed a distaste for it, and the fifth discontinued because a definite idiosyncrasy to the vitamin B complex had developed

At the present time I have over 30 patients taking this treatment, though each uses different preparations in different dosages However, I thought it best to

report the results in these few cases so that others may continue investigations along these lines

On further investigation it may be found that heavier doses of vitamin B complex orally or by injection may give better and quicker results or it may be discovered which component or components are responsible for the results obtained Also, it is probable that the hydrochloric acid acts in conjunction with the vitamin B complex to make it more easily assimilated, or it may have a good effect in itself These are questions which will have to be answered by time

J C HATHAWAY, M D, Spokane, Wash  
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## Obituaries

### JOHN HARPER BLAISDELL, M D 1887-1944

John Harper Blaisdell, 58 years of age, died suddenly on Oct 25, 1944. He graduated from Dartmouth in 1907 and from the Harvard Medical School in 1911. He served as dermatologic house officer at the Massachusetts General Hospital from July 1 to Dec 31, 1911 and then as a member of the dermatologic staff from 1916 to 1928, when he resigned. He also taught during this period at the Harvard Medical School as assistant and as instructor in dermatology



JOHN HARPER BLAISDELL, M D  
1887-1944

During his internship Ehrlich's "606" began to be generally available, and Dr Blaisdell had the opportunity of being one of the first physicians in this country to administer arsphenamine. He was also one of the first dermatologists in New England to make use of radium for cutaneous therapy.

Dr Blaisdell's particular medical interest and his greatest contribution was in industrial dermatology. He appeared frequently before the Industrial Accident Board and he was sought by numerous insurance companies and employers for opinions concerning patients with cutaneous diseases associated with occupational causes. He was interested not only in the correct diagnosis

and a just settlement in each case but in the intricacies of the rules and laws which were presented in connection with the case. His numerous reports in this field were clear and logical and often were expressed in striking phrases to emphasize special features of the case.

He had been successively secretary, vice president and president of the New England Dermatological Society. He was a specialist certified by the American Board of Dermatology and Syphilology and a member of the American Dermatological Association since 1930. He was consulting dermatologist for several hospitals in and near Boston.

He had numerous other interests. He had been a director of the Associated Hospital Service Corporation since its inception, in 1937, having been elected to this post as a representative of the Massachusetts Medical Society. He attended its meetings conscientiously and contributed actively to the success of the Blue Cross and Blue Shield. Furthermore, as a councilor for many years and as a member of the public relations committee of the Massachusetts Medical Society he was active in clarifying the relations between the Society, its members and the public. In recent years, as a member of the by-laws committee, he had an important part in formulating the by-laws under which the Society now operates. He had also been president of the East Middlesex District Medical Society. In his home town of Winchester he was much interested in civic affairs, having served as chairman of the finance committee, a member of the Board of Selectmen and chairman of the Board of Health for many years. His large stamp collection and his studies in genealogy occupied many hours of his spare time.

Dr Blaisdell was an excellent dermatologist, an able teacher and a forceful witness in court and before the Industrial Accident Board. He loved an argument, he was given to strong convictions, and he was capable of expressing himself forcefully and logically. His place in the community will be difficult to fill.

C GUY LANE, M D

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ACUTE YELLOW ATROPHY OF LIVER IN EARLY SYPHILIS, A CASE REPORT WITH SUMMARY OF THE LITERATURE MARTHA F LEONARD, *Am J M Sc* **208** 461 (Oct) 1944

After listing the mechanisms for the occurrence of jaundice in early syphilis, Leonard discusses the simultaneous occurrence of acute yellow atrophy and syphilis. Since the introduction of the use of arsenicals, there has been considerable increase in the number of cases of acute yellow atrophy associated with early syphilis, but there is said to be only 1 report of such an occurrence following treatment with oxophenarsine hydrochloride (mapharsen). Leonard points out that clinically acute syphilitic hepatitis differs little from acute catarrhal jaundice and that acute yellow atrophy associated with acute syphilis is no different clinically from that of other causes. Her patient was a 15 year old girl, in whom jaundice developed shortly after a secondary syphilitic eruption and progressed to acute yellow atrophy of the liver, death occurring about a month after the onset of jaundice. A typical Herxheimer phenomenon developed after the first injection (0.015 Gm) of oxophenarsine hydrochloride and a bismuth compound, and a much milder one occurred after the second injection (0.03 Gm) of oxophenarsine hydrochloride. Leonard reviewed reports of 31 cases of syphilitic hepatitis with jaundice in which arsenical therapy brought about rapid clearing of the jaundice. Not a single instance was found in which the use of arsenic in the presence of jaundice resulted in acute yellow atrophy of the liver. In spite of the fatal outcome for this patient Leonard believes that the evidence gathered from the literature justifies the use of arsenicals for acute syphilitic hepatitis.

GRANULOMA INGUINALE (A REVIEW OF PROGRESS) HARRY PARISER and HERMAN BEERMAN, *Am J M Sc* **208** 547 (Oct) 1944

Pariser and Beerman state that much credit must be given to certain persons and groups for their tireless efforts and prolonged study which have led to the better understanding of granuloma inguinale but that many others have also contributed. In a discussion of etiology the authors remark that most authorities are in agreement that the Donovan organism, even though it might prove not to be etiologic, is of high diagnostic value in that it is constantly associated with the disease process, they quote the conclusion of the Georgia group that the Donovan bodies are strictly tissue parasites to man. They discuss at length the various methods for identification of the organism.

Although descriptions of the clinical processes produced by granuloma inguinale are varied there is certain unanimity of opinion concerning the histologic changes which permit specific diagnosis from clinically suspected lesions. Von Hamm and D'Aunoy state that in the histologic picture of acute granuloma venereum there is a non-specific highly vascular granulation tissue which follows a brief preliminary stage of subcutaneous infiltration and which has no characteristic appearance. In the chronic hypertrophic lesions there is

a massive development of collagenous tissue which surrounds nests of plasma cells and lymphocytes. In spite of traditional teaching, the authors remark that in 2 cases removal of lymph nodes underneath extensive granulomatous involvement with this disease revealed involvement of the lymph nodes to substantiate their viewpoint.

They propose an adaption of Halty's classification and description of clinical symptoms: first, a nodular form, second, an ulcerovegetative form (which may become secondarily infected), third, a form characterized by hypertrophic lesions (with or without elephantiasis) and fourth, a cicatricial type. Systemic symptoms are usually slight or absent unless there is secondary infection, deep ulceration, rectal stricture or extension of the process to the oviducts or ovaries. The authors favor the use of antimony and potassium tartrate and state that fuadin can be used in cases in which the former drug cannot be tolerated because of reaction or in cases in which it has failed. Treatment should be continued for at least two months after complete healing, in order to avoid relapse.

USE OF FLUORESCENCE METHOD IN ESTABLISHMENT OF DIAGNOSIS AND PROGNOSIS OF PERIPHERAL VASCULAR DISEASES KURT LANGE and LINN J BOYD, *Arch Int Med* **74** 175 (Sept) 1944

Lange and Boyd report some interesting observations. They demonstrated that fluorescein when injected intravenously can be made visible on its arrival in the small blood vessels of the skin and mucous membranes by a beam of long wave ultraviolet radiation. The degree of fluorescence depends on the amount of blood flowing through that part of the body.

The method was of value in the study of embolism, thrombotic occlusion, arteriosclerotic disease and vasospastic disorders. Ulcers of the leg from a varicose vein can be judged as to the outlook for healing and skin grafting. Syphilitic ulcers of the leg have a specific picture in the fluorescein test, which distinguishes them from varicose ulcers.

ADENOMA OF APOCRINE SWEAT GLANDS (HIDRADENOMA) OF THE ANAL CANAL WILFORD L COOPER and JOHN R McDONALD, *Arch Path* **38** 155 (Sept) 1944

Cooper and McDonald describe what they believe to be the first reported case of a neoplasm of the anus arising from apocrine sweat glands, though McDonald previously reported the first description of a vulvar neoplasm whose origin could be definitely traced to an apocrine gland.

DEHYDRATION IN HISTOLOGIC EMBEDDING ELIMINATED BY USE OF A WATER-SOLUBLE SYNTHETIC PLASTIC VIRGINIA LUBKIN and MARY CARSTEN, *Arch Path* **38** 229 (Oct) 1944

Lubkin and Carsten point out some of the disadvantages of the common methods of preparing tissues for microscopic examination. They report successful use



of the synthetic resin polyvinyl alcohol as an embedding material. Advantages currently are due to a considerable reduction in the number of manipulations to which the tissue is subjected and to the fact that the lack of necessity for dehydration saves the scant supplies of alcohol and other hydrocarbons. Furthermore, the opportunity to obtain fat stains from standard tissue blocks represents a step forward.

IRRITATION AND CARCINOGENESIS I. BERENBLUM, Arch Path 38 233 (Oct) 1944

Berenblum, from the Oxford University Research Center of the British Empire Cancer Campaign, has provided a thorough and learned discussion of the relation between irritation and carcinogenesis. For this purpose he defines irritation as "unphysiologic stimulation which, being potentially destructive, elicits a continued state of reparative hyperplasia." This leads to two approaches: first, an inquiry as to whether all irritants are carcinogenic and whether all carcinogens are irritants and, second, consideration of the basic differences between hyperplasia and neoplasia and between preneoplastic hyperplasia and ordinary (reparative) hyperplasia. After thorough discussion, he concludes that not all irritants are potentially carcinogenic. He states that carcinogens of a physical nature, various radiation, freezing etc., are all irritant by any definition of the term. If by "irritation" is meant the production of a continued state of reparative hyperplasia, which is the meaning as defined in this review, then all the direct carcinogens without exception are irritants.

In conclusion Berenblum notes that the question is too simple when stated "Is irritation the cause of tumor formation?" His consideration of the problem was based on the assumption that any effect irritation might have on carcinogenesis is through the reparative hyperplasia which it induces. From known facts it is concluded that hyperplasia is an essential precursor of neoplasia. Only some, not all, irritants are carcinogenic. Therefore, preneoplastic hyperplasia must be a specific type, biologically (and, it is claimed, even morphologically) distinct from ordinary reparative hyperplasia. Carcinogenesis is probably not a single process but consists of several component phases, which may be dissociated, hence in discussing the role of irritation in carcinogenesis it is necessary to inquire whether an irritant can be responsible for some of the component phases even when it cannot produce them all. Only carcinogenic irritants can produce preneoplastic hyperplasia but once it is produced, a benign tumor can be made to appear at that site and a tumor already present can have its progress to carcinoma hastened, by the action of a variety of noncarcinogenic irritants.

FURTHER OBSERVATIONS ON THE RELATION OF THE EYE TO IMMUNITY IN EXPERIMENTAL SYPHILIS. II. THE DEVELOPMENT OF IMMUNITY AFTER PRIMARY INTRACORNEAL INOCULATION, III. THE INFLUENCE OF A NON-SPECIFIC INFLAMMATORY REACTION IN THE CORNEA ON THE DEVELOPMENT OF IMMUNITY IN THAT TISSUE AFTER INTRATESTICULAR INOCULATION. ALAN M. CHESNEY and ALAN C. WOODS, J. Exper. Med. 80 357 (Nov) 1944

After experimental studies Chesney and Woods concluded that inoculation of the cornea of rabbits with syphilitic virus is often followed by the development of immunity to the homologous strain of organisms. This immunity is imparted to the skin to a greater extent than to the cornea inoculated originally or the

opposite, uninoculated, cornea. It persists after treatment with arsphenamine. It appears to be greater the longer treatment is postponed. In two thirds of the animals there developed in both the skin and the cornea after a primary intracorneal inoculation a high degree of resistance toward a second inoculation with homologous syphilitic virus, but syphilitic disease of the cornea does not always impart to the cornea itself an absolute immunity to reinoculated homologous virus.

There was a tendency for corneas into which had been injected dead tubercle bacilli to be more refractory to a subsequent inoculation with homologous syphilitic virus than the corneas of the same animals that had not received injections of dead tubercle bacilli. In the latter study the inoculation with tubercle bacilli brought about a nonspecific inflammatory reaction with resultant vascularization, the intention being to find out whether such vascularization would render the cornea more resistant to inoculation with the homologous strain of syphilitic virus. The results were interpreted as suggestive evidence that in the syphilitic rabbit there develop circulating antibodies against the homologous strain of *Treponema pallidum*.

LYNCH, St. Paul

NEUROSYPHILIS AND THE OCULIST ALBERT C. ESPOSITO, M. Bull. Vet. Admin. 21 51 (July) 1944

In a series of 218 cases of neurosyphilis it was found on preliminary examination that 14 patients had some impairment, such as atrophy of the optic nerve field defects or failing vision, which contraindicated trypanamide therapy. Of the remaining total of 204 patients who were given this drug, a total of 26 presented symptoms of drug toxicity involving the optic nerve. Of this total, the symptoms developed in 11 patients during the first course of trypanamide and the symptoms developed in 15 patients during the subsequent courses. In general, most reactions occurred between the third and seventh injections of each course of treatment, and reactions do occur after the initial course of the drug.

It is obvious, therefore, that patients with neurosyphilis should have the benefit of collaboration between the oculist and the syphilologist.

RATTNER, Chicago

EXPERIMENTAL PROPHYLAXIS AND TREATMENT OF CHANCROIDAL INFECTION ARMAND J. PEREYRA and SIMEON LANDY U. S. Nav. M. Bull. 43 189 (July) 1944

To study the effect of penicillin on experimentally produced chancroidal infections in human beings, the authors inoculated 3 patients who were receiving penicillin for other diseases with material prepared from freshly isolated strains of *Hemophilus ducreyi*. The first patient received 10,000 units of sodium penicillin every three hours for a total of 600,000 units in seven days, and the second and third patients received 5,000 units every three hours for a total of 600,000 units in fourteen days. In all the patients the lesions developed more rapidly and extensively than in those not receiving this drug. All lesions healed readily with sulfathiazole.

The authors believe that the rapid development of chancroidal lesions in the patients treated with penicillin was due to the lethal effect on the susceptible contaminants, thereby facilitating the establishment of the *ducreyi* organisms. When a chancre fails to heal under penicillin treatment, failure may be due to a mixed infection with *H. ducreyi*, and treatment should be supplemented with a sulfonamide compound.

ROBIN, South Bend, Ind.

A CASE OF LIGHT SENSITIZATION DAVID ERSKINE,  
Brit J Dermat 56 195 (Sept-Oct) 1944

A case of light sensitization in an electric welder, aged 18, is reported because of the difficulty of treatment and because of the fact that the sensitization appeared to be of an unusual type. The patient first came under treatment for seronegative primary syphilis in June 1941. In the last few weeks of his first course of treatment scattered pustular lesions developed on the sacrum and thighs and a mild papular rash on the extensor aspects of the hands and forearms, which were exposed to the rays of the carbon arc at work. The eruption on the arms was controlled by quinine in an ointment base applied locally, but a month later a more severe scaly erythema of the face and forearms necessitated admission of the patient to the hospital. Sensitization to light of a mild type, possibly resulting from exposure to the rays of the carbon arc, was suspected, although the association with the arsenical treatment caused some concern. Hepatic tolerance tests and other investigations showed no abnormality suggesting bismuth or arsenic intoxication, but it was thought desirable to postpone his second course of treatment. A test dose of radiation from a mercury vapor lamp produced an excessive reaction, the blood picture was within normal limits, and no increased excretion of porphyrin was found at any time.

The patient left the ward after a month of treatment, but a relapse occurred within a few hours after his going into the open air, and a generalized furunculosis with an acute dermatitis developed on the exposed parts of the body. Treatment consisted of hospitalization and general tonic measures. He was discharged from the hospital only to reappear three days later with an acute edematous dermatitis of the face, forearms and hands. Treatment consisted of the administration of sulfapyridine internally, which aggravated the eruption. A tonsillectomy was advised, on the assumption that infected tonsils might be an associated factor. This was of only temporary benefit, because another relapse occurred after half an hour in the open air. Concentrated vitamin A esters were administered, but this only produced a reaction after each injection, and no improvement occurred after two months. Desensitization was next attempted with fractional doses of mercury vapor radiation. After six months two areas, each  $\frac{1}{2}$  inch (1 cm) square, could be exposed for forty seconds at 90 cm and the patient could go out into the fresh air a quarter of an hour before sunset without any reaction. This appeared to be the maximum toleration. During the twelve months occupied by these treatments two courses of treatments with injections of bismuth and one course of treatment with 30 cc of diethylamine acetarsone were given without any deleterious effects on the eruption and the Wassermann and Kahn reactions or the blood remained negative.

Further investigative work on this case showed that the patient was sensitive to the ultraviolet waveband and therefore his case differed from the recognized light sensitization of adult type in cases of which the patient is sensitive to rays of a wider band including at least a proportion of longer wavelength. This case was further differentiated from the usual kind in that the adult type of sensitization is frequently associated with evidences of hepatic insufficiency and such subjects are not protected by quinine or tannic acid and are usually benefited by injections of concentrated vitamin A esters.

SOME OBSERVATIONS ON SKIN-DISEASES WITH THE  
ARMY IN INDIA ALLAN BIGHAM, Brit J Dermat  
56 199 (Sept-Oct) 1944

The most common cutaneous diseases seen in India, according to the author, are trichophytosis and scabies. These two head the list in incidence on an all season basis, but are leveled by prickly heat, with its frequent complications, and by tropical (bullous) impetigo during the monsoon period.

British troops suffer far more from tinea interdigitalis than do the Indian troops. The great majority of Indian troops had not been accustomed to wearing boots before joining the army. Thus they have tougher feet, and their toes are not malformed and cramped together but are properly spaced, allowing for quick dispersal of sweat and heat.

British and Indian troops suffer equally from tinea cruris and tinea circinata, but, given equal treatment, it is much easier to clear the Indians of their fungous disease than the British, because the pigmented skin appears to stand stronger applications without reaction than does the white.

Tinea circinata presents no diagnostic difficulty once the initial surprise at the size of the lesion has worn off. It is not uncommon to see the whole chest and abdomen of a large healthy soldier covered by one lesion of tinea circinata.

Scabies, the next most common cutaneous disease, is practically never seen uncomplicated. In India, a breach of the epidermis almost automatically results in secondary infection unless great care is taken. The difficulty of giving such care to troops on the move and in the jungles is easily understood. Therefore, ecthyma is as common as scabies and the more serious complications, such as lymphangitis, cellulitis and infected lymph nodes, are frequent.

The initial impetigo lesion is a true vesicle which, instead of rupturing almost at once to form a crust, goes on to form a bulla. A typical well developed lesion will show a layer of pus cells covered by a layer of serum in a flaccid bulla. It frequently starts in the axillas or groins and in the sweat, friction or pressure areas, and once begun it can cover large areas in a short time. It is by no means uncommon to find prickly heat, bullous impetigo and tinea of all types in the same patient, and in this association the tinea spreads rapidly.

BLUEFARB, Chicago

CALCINOSIS UNIVERSALIS IN AN INFANT B SANCHEZ  
SANTIAGO and R PEREIRAS, Arch de med inf 11 1  
(Jan-March) 1942

The authors review the literature on calcinosis universalis, with special reference to the etiology, and present a clinical case. A 14 month old white boy had a history of lumbar pain when lifted, generalized edema and fever reaching 39 C (102.2 F) at the age of 5 months. On his admission to the hospital he had numerous disseminated hard nodules and plaques, several open abscesses and pronounced generalized spasticity. Roentgenograms revealed calcareous deposits throughout the body. The blood chemistry was normal. There was slight anemia, with a red cell count of 2,900,000. Biopsy confirmed the diagnosis of calcinosis universalis.

BRIEFSCA Zamora, Mich., Mexico  
[AM J DIS CHILD]

# Society Transactions

## NEW YORK DERMATOLOGICAL SOCIETY

A BRNSON CANNON, M D, *President*

GEORGE C ANDREWS, M D, *Secretary*

March 28, 1944

### Generalized Progressive Scleroderma Presented by DR HOWARD FOX

L R, a Jewish housewife aged 39, first noticed a burning sensation in her chest about five months ago. It appeared suddenly and without apparent cause. She had previously been in good health. She soon noticed brown streaks on the front of the thighs and spent ten days in Mount Sinai Hospital (service of Dr Isadore Rosen), where a diagnosis of scleroderma was made. The eruption gradually spread until at present it is generalized, symmetric and profuse, involving the trunk, the neck, the upper extremities as far as the wrists and the thighs. The hands, face and legs are unaffected. The skin is yellowish, shiny and hidebound in the affected areas. There is no tenderness on firm pressure. The patient complains of a burning sensation in certain areas and itching in others. She looks and feels sick.

At Mount Sinai Hospital, biopsy showed scleroderma. Results of other laboratory examinations at this hospital were as follows. The Wassermann reaction of the blood was negative. There was a moderate, simple anemia. A chemical examination of the blood showed 115 mg of sugar and 112 mg of calcium per hundred cubic centimeters of blood and 17 King-Armstrong units of phosphatase. A urinalysis, electrocardiogram and a roentgenogram of the chest showed no abnormalities. The basal metabolic rate was  $-7$  per cent.

#### DISCUSSION

DR FRED WISE. I agree with the diagnosis and should like to call attention to the possibility of involvement of the lungs in this disease. A roentgenogram of the lungs should be made.

DR A BRNSON CANNON. Dr Fox has intimated that the classification of scleroderma should be studied and reviewed, and I think that equally careful thought should be given to the matter of treatment. A universal scleroderma involving the entire cutaneous surface, with or without sclerodactylia, is an entirely different problem in treatment from that of the manifestation of the disease which one sees here today. In fact, a universal scleroderma is a very difficult and well nigh impossible disease to cure, whereas I should think that the prognosis in this case is bright. I believe that this patient should respond satisfactorily to roentgen irradiation, almost as well as a patient with morphea treated with radiation, plus, perhaps some thyroid if it is found to be indicated, as most observers believe that it is.

DR HOWARD FOX. The chief point of interest in this case is the rapid spread of the eruption within a few months. Although the sudden appearance was like that of sclerodema adultorum, it was not preceded by any febrile or other disease and pigmentation was present. I hope that Dr Cannon's favorable prognosis will be fulfilled. As for treatment, I have always been skeptical about the value of any specific treatment for this disease.

### A Case for Diagnosis (Psoriasis of the Palms and Soles, Keratoderma Climacterium?) Presented by DR GEORGE M LEWIS

Mrs G S, aged 66, first had a rash on the palms in mid January 1944. This gradually spread to involve the palms and soles and to a lesser degree the dorsa of the fingers. The affected skin is reddened and scaly, with many painful fissures, particularly near the joints. No evidence of cutaneous lesions is found elsewhere on the scalp or body. There is considerable pain, which the patient localizes in relation to the fissures and also in the joints.

#### DISCUSSION

DR GEORGE M MACKEE. I am inclined to agree with the diagnosis of psoriasis. In my experience psoriasis which is limited to the hands and feet is apt to be exceedingly stubborn. It is likely to resist conventional remedies, such as chrysarobin and safe therapeutic doses of roentgen rays. I have tried everything that has been recommended for such patients, and as a rule I obtain best results with crude coal tar (3 per cent ointment locally) and ultraviolet irradiation or heliotherapy of the entire body every day (Goeckerman treatment).

DR R H RULISON. I agree with Dr MacKee. In cases of this type I have sometimes had surprising success with crude coal tar ointment.

DR HOWARD FOX. In treating psoriasis or other diseases of the palms with roentgen rays, one should be extremely cautious, as this area is radiosensitive owing to the lack of sebaceous glands. An eruption like this would be suitable for strong ointments of chrysarobin or dihydroxyanthranol, preferably covered by an impermeable substance, such as a rubber glove. I still treat some patients with obstinate psoriasis with autoserotherapy and think that, although the rationale of this procedure is hard to explain, it often increases the action of chrysarobin. However, I have obtained good results only when about 50 cc of blood was taken and the serum obtained by centrifuging and injected intramuscularly. I have never seen any favorable results from autohemie therapy when small amounts of blood, such as 5 or 10 cc, were used. As stated in my article following the work of Gottheil and Satenstein (*Human Serum and Blood in the Treatment of Psoriasis and Other Skin Diseases, J Cutan Dis, incl Syph, N Y* **33** 616 [Sept] 1915), the good effects of taking 50 cc of blood may be due simply to the venesection.

DR PAUL E BECHET. I agree with the diagnosis of psoriasis, but I feel more positive about it than those who have discussed the case. The lesions are typical of psoriasis in that location, and in my opinion no other diagnosis seems plausible. The age of the patient should not influence the diagnosis. I have not infrequently seen psoriasis occur in elderly persons and have occasionally observed even lupus vulgaris in patients over 60.

DR EUGENE F TRAUB. I believe that this patient has psoriasis of the palms and soles. Her eruption resembles the type which Dr Throne thought was rebellious to treatment because of the patient's previous ingestion of arsenic. Whether there is such a history in this case I do not know, but Dr Throne felt that not infrequently such patients were benefited by the administration of sodium thiosulfate. Recently I have had excellent re-

sults in some cases of involvement of the hand by using Duret's balsam. This is a preparation difficult to make, but the Doak Company, of Cleveland, has made it, and it should be of great benefit in Dr Lewis' case. Duret's balsam consists of a mixture as modified according to the formula in the "Text-Book of Dermatology" by Darier: resorcinol, menthol, guaiacol, cadimene, precipitated sulfur, liquid wood tar, sodium borate, camphor, castor oil, glycerine, acetone and hydrous wool fat.

DR A BENSON CANNON I am in agreement with the diagnosis of psoriasis, but I should be on guard for the possibility of its being lichen planus. I say that because of the isolated lesions on the palms, the type of scaling of the palms and the shiny beefy red papules on the fronts of the wrists. She also has a beefy red, smooth small tongue, a condition which is often spoken of as being evidence of an avitaminosis. However, granted that the disease is psoriasis the question of therapy comes up, and I repeat what I have stated here before. The only therapy I have ever seen that cleared a plantar and palmar psoriasis is injections of crude liver, a high caloric high vitamin diet, generalized ultraviolet irradiation and crude coal tar ointment.

DR GEORGE M LEWIS It is interesting that no one suggested the administration of arsenic, which indicates that this drug is no longer as favored a remedy as formerly.

### Onychomycosis Due to *Trichophyton Purpureum*

Presented by DR GEORGE C ANDREWS

P K, a man aged 23, has had recurrent attacks of a vesicular, crusted, scaly, eczematous, sharply demarcated psoriasiform eruption on the palms and soles of four years' duration. From the finger and toe nails, which are thickened, stippled, discolored and brittle like the nails in psoriasis, I have repeatedly recovered masses of fungi, which on culture are *Trichophyton purpureum*. With the usual antiparasitic remedies, the cutaneous eruption has responded to treatment but the affected nails have not. The nails have been treated with roentgen rays, 10 per cent propionic acid in alcohol and lotions containing thymol, salicylic acid and iodine.

The case is presented for therapeutic suggestions.

#### DISCUSSION

DR GEORGE M MACKIE Years ago I tried various forms of treatment for onychomycosis without encouraging results—topical remedies, heat, roentgen rays and avulsion. Even after avulsion the new nail was usually infected. Recently my associates and I have been removing the nail by blunt dissection and curettage and then treating the nail bed twice a day with applications of modern penetrating vehicles containing a fungicide. Thus far the results have been satisfactory.

DR PAUL E BECHET I should like to get some expression of opinion as to the therapeutic value of roentgen rays in treating fungous infections of the nails, as my own experience has been somewhat contradictory. I have had unusually good results in some cases, yet in others there has been a recurrence a year after an apparent cure, and in a few there was no response to treatment.

DR GEORGE M LEWIS I think that the point brought up by Dr Bechet is interesting and can be explained on the basis of the organism that is causing the disease. I do not think that roentgen rays ever help *T. purpureum* infections but they certainly do in *Trichophyton* species infections. At New York Hospital total

avulsion of the nails under anesthesia has been given up. It is remarkable how much nail one can remove with a scalpel without an anesthetic, and particularly, when the nails are crumbly. It takes about five minutes to remove the nail, time well spent because in it one removes material that one cannot well treat. It certainly obviates the possibility of infection with pyogenic organisms. We follow up with use of chrysarobin or dihydroxyanthranol or one of the strong fungicides. We get fairly good results. There are some recurrences of course, but this is the method we generally use now and have been using for some time.

DR HOWARD FOX I intended to bring up the question of avulsion of nails for the treatment of onychomycosis, in view of the recent statement made by Dr Caro (Caro, M R. Fungus Infections of the Foot, *J A M A* 124 751 [March 18] 1944) that he did not approve of this method because of the likelihood of recurrence. Avulsion of nails for ringworm or favus was formerly carried out in a wholesale manner at Ellis Island at a time when a million immigrants were arriving each year. As the patients would have been deported if treatment had been refused, they willingly submitted to avulsion of the nails under a general anesthetic. The matrix was then treated with an escharotic, which prevented recurrence and also destroyed the regrowth of the nails.

I should like to ask Dr Lewis' opinion about the value of constant scraping of infected nails, followed with the application of ointment of benzoic and salicylic acid. Mr Hodges, the well known pioneer in mycology, is said to have cured his own onychomycosis with this method in six months.

DR GEORGE M LEWIS Avulsion of the nails should not be left to the patient. The patient never scrapes deeply enough to get rid of sufficient nail.

DR A BENSON CANNON My experience has been similar to that of Dr Lewis. In former years I removed all infected nails. When I was with Dr Fordyce, I recall removing all the finger nails and toe nails in a woman at one sitting. She had a perfect regrowth of nails with no reinfection, and the reinfection she had had in the groins was also cleared up. In more recent years I have not found such drastic treatment necessary. I have been convinced that surgical cleanliness and trimming off of dead portions of the nail and the dead skin around the nail (which can be done only by a physician) followed by the application of various antiseptics will invariably clear the infection. It will do this in a surprisingly short time—within a few months—and it is well worth the effort. I do not believe that one can leave it to the patient to do, as Dr Lewis has just stressed, it is entirely dependent on the physician. I use not only nail clippers but a hook curet to get underneath the nail.

### A Case for Diagnosis (Diffuse Telangiectasia of the Trunk and Upper Extremities?) Presented by DR FRED WISE

S W, a woman aged 34, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 4, 1944, presenting lesions of seven years' duration. The patient has been suffering from hay fever for thirteen years. Five years ago, on two occasions, uniform swellings of the eyelids, hands and feet developed after ingestion of acetylsalicylic acid and a proprietary preparation containing acetophenetidin. These swellings lasted overnight. She complains of some itching and weakness after exacer-

bation of the eruption The menstrual periods are regular but scanty

The patient has two children, aged 12 and 7 respectively The older child since babyhood has had allergic dermatitis of the cubital regions and the back of the neck

The patient's eruption first appeared suddenly on the chest and arms during the fourth month of pregnancy with the second child It then resembled the present eruption, which is made worse by heat and by anger The eruption on the chest and the extremities has never entirely disappeared The eruption on the rest of the body occurs only during excitement and on exposure to heat but disappears within an hour or two with relaxation When the patient first came to the clinic, her face was intensely erythematous, suggestive of primary polycythemia vera

The eruption consists of diffuse erythema and conspicuous telangiectases, situated on the upper portion of the chest and neck and in both cubital areas On March 24 the eruption had almost entirely faded Only scattered fine telangiectases were seen on the front and back of the chest and on the upper limbs They faded on diascopic pressure

The results of the routine laboratory tests were negative, the platelet count and the bleeding and coagulation times were normal Results of routine chemical examination of the blood were normal except for 17 mg of urea nitrogen per hundred cubic centimeters of blood (normal, 10 to 15 mg) The result of a tourniquet test was negative The eyegrounds were normal A general physical examination showed no abnormalities except for overweight Tests for allergy performed five years ago were said to have given negative results

A histologic section examined by Dr Charles F Sims was diagnosed as "vasculitis" The description was as follows The epidermis revealed no noteworthy changes The vessels of the upper part of the corium were moderately dilated, their walls were edematous, and in many instances their intimal nuclei were swollen The lumens were somewhat occluded and in places completely closed There was some proliferation of adnexa cells

#### DISCUSSION

DR EUGENE F TRAUB It would be difficult from one examination to make a definite diagnosis for this patient, but the case does not seem to me to be one of simple erythema, and I believe that such a designation for this particular eruption is incorrect The impression which I get is that this eruption either consists of tiny little blood vessels, a sort of telangiectasia or possibly is a purpuric eruption of peculiar character There seems to be a reticulated vascular network and not a diffuse erythema of the skin The possibility that this type of vascular change is caused by syphilis should be considered, as I believe that syphilis does occasionally produce peculiar changes such as are seen in this patient Should the eruption prove to be purpuric, a drug eruption might also be considered However, I feel certain that the eruption is more likely a result of change in the blood vessels rather than a purpuric type of lesion

DR PAUL E BECHT I agree with Dr Traub's interpretation of the case I distinctly saw telangiectasia, it was in fact annular and lacelike The question of exposure to actinic rays may have a part The patient is pale, of course but it may be that she has had at some time or other sufficient exposure to actinic or ultraviolet rays to cause the disease under discussion

DR HOWARD FOX Telangiectases do not come and go and as most of the redness disappears under

pressure, I should call this a recurring toxic erythema of unknown cause

DR FRED WISE Some of the red lesions disappear spontaneously

DR R H RULISON I agree with Dr Traub that to use the term "erythema" in diagnosis does not give a good description I think that the patient has a hair-trigger vasomotor system and irritable capillaries She herself said that the eruption is like an eruption of measles I believe that this is more descriptive than to say that it is an erythema I have no idea of the cause nor any suggestions for treatment

DR GEORGE C ANDREWS The unusual feature of this case seems to be the history of frequent recurrences The patient apparently has a toxic erythema of gastrointestinal origin

DR FRED WISE The histologic picture shows well defined telangiectases Many dermatologists think that this form of eruption is related to a thyroid disturbance

#### Pachyonychia Congenita Presented by DR HOWARD FOX

S D W, a man aged 20, was presented before the Society sixteen years ago (ARCH DERMAT & SYPH 18 794 [Nov] 1928) and was last seen by me ten years ago He is to appear soon before his draft board for possible induction into the army

Since the original presentation, there has been little change of importance The nails grow in the same manner, and he still has calluses on the bearing surfaces of the feet His chief complaint is the appearance of blisters when he walks too much or sweats too freely There are now only a few spinous lesions, which were formerly present, and apparently there is no diminution of lesions of the keratosis pilaris type on the extremities A large pea-sized wart is still present, near the olecranon of the left side There have never been any lesions of the mouth The patient is a vigorous-looking young man in apparent good health

#### DISCUSSION

DR GEORGE C ANDREWS This is the patient I described in 1927 Of course, he has grown considerably since then With regard to the skin and nails, they look about the same as they did then He does not now have the large bullae on the heels that were formerly there

DR EUGENE F TRAUB This patient presents a number of peculiar lesions somewhat resembling keratosis pilaris, and some of the lesions on the shoulders and neck are hyperkeratotic For this reason I wonder whether vitamin A in large doses might help, at least to clear the eruption on the body and possibly to have some beneficial effect on the hyperkeratoses of the feet as well

DR GEORGE C ANDREWS I have treated patients with pachyonychia congenita with large doses of vitamin A without benefit

DR EUGENE F TRAUB Certainly this type of therapy could do no harm, and vitamin A in large doses over a considerable period might have benefit

DR HOWARD FOX Treatment of the keratosis pilaris lesions would not interest this patient, as they cause no inconvenience He is greatly troubled by bullae, which occur on the soles after considerable walking or perspiring The lesions are similar to those of epidermolysis bullosa, reports of cases of which have recently been published by medical officers in the Army He

appeared before his draft board recently and was rejected

DR EUGENE F TRAUB According to Peck, Chargin and others, some hyperkeratotic eruptions, as well as Darier's disease, which have always been included in the congenital anomalies, are actually improved by vitamin A medication. While this type of therapy would have to be empiric, one can tell only after a conscientious trial whether or not improvement has taken place.

DR PAUL E BECHET I have always felt that keratosis pilaris is congenital and related to a mild ichthyosis. If this is correct, I cannot see how it would be possible to effect its disappearance by the administration of vitamin A.

#### A Case for Diagnosis (Arsenical Keratoses of the Palms and Soles, Trophic Ulcer of the Foot?)

Presented by DR A BENSON CANNON

A P, a married Negro woman aged 54, who worked in a cigar factory, was admitted to Presbyterian Hospital on March 21, 1944, complaining of a "corn" on the left sole for twenty-one years, which had become much larger in the preceding year and a half and painful. She has worked since the age of 13 in a tobacco factory in Tampa, Fla., stripping the leaves from Cuban tobacco stems by hand. She said that a "corn" came on the left sole twenty-one years ago, which slowly enlarged and became so painful on walking that she had it removed by excision eighteen months ago. The "corn" returned after the operation and remained painful to pressure. She applied a proprietary liquid corn remover for a year without any relief.

There is no past history of any serious infectious diseases. She gave no history of any prolonged ingestion of drugs by mouth and no history of any arsenical medication of any kind. Because of anorexia she has lost about 25 pounds (11.3 Kg) in weight during the past year.

On the left plantar surface in the midlateral location is an elevated, fungating, foul-smelling, sharply demarcated keratotic lesion, about 3 to 4 cm in diameter, with a sunken necrotic center. A similar but smaller lesion, evidently in connection with the larger one, is on the lateral side of the foot about 3 cm distant. This smaller lesion is also fungating and is about 1.5 cm in diameter. No surrounding inflammation or edema is present, but a depressed pigmented area is found near the lesion on the lateral side of the foot. The areas surrounding these tumors are not painful to palpation, neither is any infiltration discovered. Scattered over the plantar and palmar surfaces are discrete elevated keratotic masses, 1 to 2 mm in diameter, which can be removed readily. No enlarged nodes are present in the groins. The remainder of the cutaneous surface is clear. Except for a blood pressure of 180 systolic and 86 diastolic, the physical examination reveals essentially normal conditions.

Biopsies of a left inguinal lymph node and of the edge of the lesion on the left foot before admission were diagnosed as chronic lymphadenitis and plantar hyperkeratosis respectively.

The blood count showed 152 Gm of hemoglobin (105 per cent), 5,250,000 erythrocytes and 16,450 leukocytes, with 76 per cent polymorphonuclear leukocytes and 24 per cent lymphocytes. The urine contained albumin (1 plus) and an occasional erythrocyte. The Kline reaction was negative. Fungi could not be found on examination or culture. A smear from the lesion showed no acid-fast organisms. A roentgenogram of

the left foot showed an irregular sinus tract beneath the fourth and fifth metatarsal bones. Lesions suggestive of periostitis were present at the base of the fourth metatarsal. Results of examination of the blood for arsenic have not yet been reported.

#### DISCUSSION

DR GEORGE M MACKEE The tentative diagnosis of trophic ulcer may be correct. I have seen plantar warts and callosities behave that way in diabetes. However, I understand that diabetes has been ruled out in this case. As Dr Cannon stated, arsenical keratosis and epithelioma have been considered but apparently ruled out by biopsy.

DR GEORGE M LEWIS This is a difficult case to discuss because we are thinking of so many diverse conditions and really not satisfactorily ruling out any of them. I cannot help having the impression that the possibility of a malignant condition must be considered, and this applies particularly to the lesion on the sole. Of course the presence of fistulas and the area on the outside of the foot would not fit in well with that impression. Also, I am not at all certain that an actinomyces burrowing deeply into those tissues would not present this picture.

DR EUGENE F TRAUB I agree entirely with Dr Lewis except that the first thing I thought of, because of the fistulas, was actinomycosis or some type of deep fungous infection. It is difficult to conceive that a cancer beginning on the foot would produce the changes seen in this patient, especially the sinus formation. Therefore, I believe that a deep fungous infection or some other type of deep-seated infection must be given first consideration in this case.

DR PAUL E BECHET In my opinion, the possibility of malignant disease is sufficiently justified to warrant the radical excision of this lesion. Further histologic studies could then be made to prove or disprove the presence of malignant change. In as deep and large a lesion as the one under discussion, malignant changes might not be found until a large number of sections have been examined. I have repeatedly observed typical epitheliomas clinically, with sections showing only inflammatory changes; it was only when a large number of sections were examined that the histologic picture assumed a malignant aspect.

DR HOWARD FOX The lesions on the borders of the palms are without doubt arsenical keratoses, and I think that the probability is that the lesions on the sole are due to the same cause. The large lesion suggests an epithelioma and should be excised.

DR FRED WISE I feel that further investigations should be made to exclude tuberculosis.

DR JOHN C GRAHAM I understand that the fourth metatarsal bone is involved, and it seems to me that this type of sinus formation could well come from an underlying osteomyelitis or some other osseous lesion or a fungous infection. It seems to me that idea would be worth investigating further, with excision or exploratory operation.

DR R H RULISON It seems to me that the only explanation that would account for the lesions both on the feet and on the hands is the one made by Dr Fox.

DR GEORGE C ANDREWS I agree with those who consider this to be either an actinomycotic infection or a tuberculous infection. I realize that the lesions on the hands are typical of arsenical keratoses and the lesions on the feet are typical of arsenical keratoses,



but I cannot imagine an epithelioma of the foot consisting of multiple draining sinuses. The patient has an ulcer on the sole and lesions on the side of the foot, not connected in any way. There are multiple openings with normal-looking skin between. Scrofuloderma or actinomycosis seem more likely diagnoses than epithelioma. In long-standing deep actinomycotic infections of the feet it is sometimes difficult to find the fungus.

DR FRED WISE: Is there a history of contact with arsenic?

DR A BENSON CANNON: Yes. The tobacco is sprayed with arsenic several times a year, and the patient's job is to strip the leaves. She has been transferred to Dr Stevenson's service for excision of the lesion in toto and for skin grafting. The surgeons regard this ulcer as a simple inflammatory process.

#### Chronic Recurrent Papulopustular Dermatitis Related to a Vitamin Deficiency Presented by DR R H RULISON

Mr H V, a 46 year old bus driver, has had his eruption for eight years. When first seen, in 1939, he had a papulopustular eruption which involved the hands, forearms, lower portions of the arms and axillas. Since that time, there has been involvement of almost all the body at different periods, the most obstinate eruption being on the knees, the anterior aspects of the thighs, the popliteal spaces, the lower part of the abdomen and the buttocks. No seasonal improvement in the eruption has been noticed. At times the face has been the site of a moderately extensive eruption of the same character.

Examination by an internist disclosed no significant abnormality.

Many forms of local and internal therapy have been used, often with temporary improvement. Roentgenotherapy has been uniformly helpful but not curative.

On Dec 1, 1942, capsules containing vitamin A 5,000 U S P units, vitamin D 500 U S P units, thiamine hydrochloride 1 mg, riboflavin 2 mg, ascorbic acid 30 mg and nicotinamide 10 mg were prescribed. The eruption entirely cleared up in two or three months, and the patient remained well until late September 1943 when a recurrence developed. He had stopped taking the vitamin preparation in the spring of 1943. In December 1943 he resumed use of the vitamin preparation, and the dose was increased to 3 capsules daily. By the middle of February he was nearly well. At this time he had taken all his capsules, and he failed to renew his prescription for two or three weeks. The eruption reappeared. Medication was again resumed, and the eruption is now rapidly disappearing.

The patient has at various times tried other vitamin compounds recommended by friends and has found them unsatisfactory.

The only local application has been phenolated petrolatum and an occasional small dose of roentgen rays.

The case is presented as an instance of a chronic, recurrent, papulopustular dermatitis due to vitamin deficiency, which clears completely as long as the lacking vitamins are supplied.

#### DISCUSSION

DR HOWARD FOX: I think that this case is worth putting on record. On three occasions, the eruption has disappeared or greatly improved after the patient has taken vitamins and has then recurred after this treatment was stopped. In view of the enormous amounts of vitamins taken at the present time, there are few diseases of the skin that show any favorable response to their administration.

DR EUGENE F TRAUB: This patient apparently has several different types of eruption, one of which certainly seems to be a contact dermatitis from carrying a large leather wallet in an inside coat pocket or a shirt pocket, giving rise to the lesion on the trunk. The other lesions, which apparently are much improved now, may possibly be related to a vitamin deficiency, but I believe further observation and study of the patient are necessary before the case can be accepted as one of a papulopustular dermatitis representing a vitamin deficiency.

DR GEORGE C ANDREWS: The presence of many pustules and abscesses suggests a staphylococcic infection to me. He may have some focus of infection. Certainly this patient's teeth are in bad condition, and most of them should be extracted. In spite of the history of the results of vitamin therapy, I should be inclined to see that he has his teeth fixed.

DR R H RULISON: This patient has promised for years to have his teeth fixed. So far as a thorough investigation with reference to vitamin content is concerned, he has neither the time nor the money for it, and I cannot hospitalize him, because he has a family to support and must earn a living. The eruption today shows only the smallest fraction of what he has had at times. He has had it almost completely covering his body. With regard to Dr Traub's point about the eruption on the side of the chest. For years this man had a large patch on the front of one thigh until I found that he carried a large bunch of keys which caused pressure on that area. The patch on the breast shows the most activity now and is the most recent patch he has. He carries a number of things in the pocket of his coat, and I told him to shift them. Since then the eruption has improved. In the popliteal spaces and the pubic areas and on the thighs and the axillas, the eruption has been pustular. He is not getting large doses of vitamin A. He is taking a mixed preparation of vitamins with not very large doses of any one vitamin. This is the third time that his eruption has almost cleared while he has been taking this vitamin preparation, and it has not cleared with anything else I have tried.

#### A Case for Diagnosis (Angioma, Angiosarcoma?) Presented by DR FRED WISE

A F, a boy aged 10, was referred to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital by Dr Phyllis S Kerr. He presents, 2 inches (5 cm) inside the line of the right nipple, a dark purplish, soft, painless growth, the size of a large pea, surrounded by a lighter purplish blue zone, 2 cm in diameter. The lesion is of two months' duration. It is composed of a faintly erythematous disk, about 3.1 cm in diameter, with sharply defined borders. Within the center of this discoid area is an elevated, soft, hemispherical, pea-sized angioma that is purplish red. On diascopic pressure the erythematous vascular zone disappears completely, but the central elevated lesion only becomes fainter in color. The lesion is painless.

#### DISCUSSION

DR GEORGE M MACKEE: Dr Wise presented this case for diagnosis but made two tentative diagnoses, the second of which was nevus tardus, with which I am rather inclined to agree. The lesion disappears almost entirely on firm pressure. I suspect that it is an angioma or, at least, angiomatous.

DR GEORGE C ANDREWS: I do not know what the lesion is. It may be an angioma.



DR GEORGE M LEWIS I cannot make a definite diagnosis or give a definite opinion, but from a distance it looked like a lesion resulting from a bite, perhaps causing vascular damage resulting in this nevoid change.

DR EUGENE F TRAUB If this is a type of vascular nevus, it certainly must be an unusual one. The nodule seems to be inflammatory, with some vascular changes, and for this reason I should suggest the diagnosis of an angiosarcoma. This type of nodule is accompanied with considerable inflammatory reaction and some change in the blood vessels. That might explain the peculiar appearance noted in this nodule. Ormsby and Montgomery (Ormsby, O S, and Montgomery, H. *Diseases of the Skin*, ed 6, Philadelphia, Lea & Febiger, 1943, p 802-803) state that when the lesions are few the clinical distinction of Kaposi's sarcoma from various granulomas, angiosarcoma, melanoepithelioma and lymphoblastoma may be difficult. They also state that the changes in Kaposi's sarcoma may at first be inflammatory, eventuating in true malignancy. They further state that the classification of cutaneous sarcoma varies and that there is no uniform agreement as to the tumors which belong in this group. Most authors do not recognize malignant endothelioma. Therefore, lesions described under "hemangioendotheliomas" and those designated "periepitheliomas" could be grouped under the term "angiosarcoma."

DR JOHN C GRAHAM I believe that it is a nevus tardus.

DR GEORGE C ANDREWS I should leave this lesion alone and watch it for a while. The presenter is not afraid it is malignant, is he?

DR GORGE M MACKEE The lesion can be excised. I suggest removal of the entire lesion because of the uncertain diagnosis. It may be angiosarcoma.

NOTE—Histologic examination subsequent to presentation showed a hemangiopericytoma.

#### Angiokeratoma (Unilateral Nevus) Presented by DR FRED WISE

R M, a boy aged 9, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb 26, 1944, presenting lesions of two years' duration. On the outer aspect of the left leg, thigh and buttock are numerous discrete, dark purplish red, elevated lesions, from a small pinhead to a barleycorn in size. Their surfaces are capped with firmly attached tiny hyperkeratotic clumps of scales, which when scratched off leave small bleeding points. The pattern of the eruption as a whole is that of a unilateral nevus.

#### DISCUSSION

DR HOWARD FOX This is an unusually profuse eruption of tiny angiomas, covered by keratotic scales. The eruption is well named.

DR FRANK C COMBES I agree with the diagnosis.

DR JOHN C GRAHAM I agree with the diagnosis and am glad to have seen this patient.

DR GEORGE M MACKEE This is the most widespread and the best case of angiokeratoma I have ever encountered.

DR FRED WISE I believe that most angiokeratomas are of a nevoid nature.

#### A Case for Diagnosis (Calcinosis Cutis, Osteopoikilosis?) Presented by DR GEORGE M LEWIS

W E, a man aged 37, first came to the New York Hospital on Jan 17, 1944, complaining of pain in the left calf which radiated up to his hip. This began ten

years ago, with occasional attacks of pain after exercise and increasing in severity with shorter periods of freedom until December 1943, when the pain was almost continuous. He has also noticed a hard, firm plaque on the lateral aspect of the left thigh for several years. On examination a stony hard area about 5 inches (12.7 cm) in diameter is noted in the subcutaneous tissue of the outer aspect of the left thigh.

Roentgenographic examination of the pelvis, right femur, both legs and lumbar portion of the spine revealed numerous small areas of increased density at the ends of the long bones, in both ilia and in the ischia and the pubic rami. My impression is that this is osteopoikilosis. Biopsy of a section from the left thigh revealed calcification with little evidence of inflammation. The Mazzini reaction was negative. The urinalysis and blood count gave normal results.

#### DISCUSSION

DR J GARDNER HOPKINS I may be mistaken, but I think that this is the disease of the bones which roentgenologists call "spotty bones" or "osteopoikilosis." The lesions are probably minute fibromas in the bones. Some years ago Dr Helen Curth made a report on dermatofibrosis lenticularis disseminata (Curth, H. *ARCH DERMAT & SYPH* 30 552 [Oct] 1934), which is rather frequently associated with this bone disease. I do not recall that there were any cases of calcinosis in her series.

DR GEORGE M LEWIS In this patient there are no fibromas and no evidence of any lesions of that type.

#### Pityriasis Rubra Pilaris Presented by DR HOWARD FOX

Miss J L, previously presented (*ARCH DERMAT & SYPH* 49 69 [Jan] 1944), shows a splendid result from daily administration of vitamin A in doses of 200,000 U S P units. There is still considerable scaling of the scalp, but most of the generalized and profuse eruption has disappeared under treatment with vitamins.

#### DISCUSSION

DR FRED WISE It would be interesting for me to supplement Dr Fox's report on his case of pityriasis rubra pilaris. There has been a young soldier in the wards of the New York Post-Graduate Medical School and Hospital for six weeks with an eruption of pityriasis rubra pilaris which covered his entire body. He had had enormous doses of vitamin A without the slightest benefit, it had absolutely no effect on his eruption. He was discharged as unimproved.

#### Possible Lupus Erythematosus Presented by DR EUGENE F TRAUB

P W, a man aged 45, was previously presented before this society on Feb 29, 1944 (*ARCH DERMAT & SYPH* 51 290 [April] 1945).

The patient submitted a report from a commercial laboratory that some type of epidermophyton had been obtained from scrapings taken from near the tip of the nose. Because of this, the patient was sent to Dr George M Lewis, as my laboratory examination had given entirely negative results as far as fungi were concerned. Dr Lewis took specimens for culture and has reported that thus far his results have been negative.

#### DISCUSSION

DR GEORGE M LEWIS Nothing was found on direct mount, and there has not been enough time yet for cultures to grow.

SAN FRANCISCO DERMATOLOGICAL  
SOCIETYJOHN H FANNING, M D, *Chairman*FRANCIS M KEDDIE, M D, *Secretary-Treasurer**April 10, 1944*Lichen Verrucosus et Reticularis (Kaposi), Poro-  
keratosis Striata (Nékâm), Morbus Monili-  
formis Lichenoides (Wise and Rein) Pre-  
sented by DR HIRAM E MILLERMrs E A M, a 38 year old white woman, is pre-  
sented from the dermatologic clinic of the University

course of roentgen ray treatments, have seemingly served only to aggravate the eruption. She has been taking large doses of vitamin A (150,000 U S P units daily) since January 1944, with some reduction in the hyperkeratosis of the lesions on the extensor aspects of her forearms. She has lost 100 pounds (45 Kg) in the past year, while on a reducing diet. She has always been overweight, her average weight being from 220 pounds (99.8 Kg) to 240 pounds (108.8 Kg). A coincidental diagnosis of chronic cholecystitis was made after her admission to the University of California Hospital, on March 6, 1944. At that time the urine was normal, the erythrocyte count was 5,250,000 and the leukocyte count was 6,000, with polymorphonuclear cells 58 per cent, lymphocytes 40 per cent, monocytes 2 per



Fig 1—A, eruption resembling lupus erythematosus and, B, linear lichenoid keratotic areas on the arm

of California Hospital. She has had a "sensitive" skin all her life. From the age of 10 to the age of 24 she noticed that heat or exercise would cause flushing of her skin, with the appearance of red blotches and streaks on the flexor aspects of her arms. About twelve years ago her first pregnancy terminated in stillbirth, and the eruption became more definite and persistent at that time. It has become progressively worse, with partial spontaneous exacerbations and remissions in the past five years. There have never been any subjective symptoms. Many therapeutic attempts, including a

cent and no eosinophils or basophils. The basal metabolic rate was — 24 per cent.

There are three types of lesions. On the face is a reddish scaly type, not unlike that of disseminated lupus erythematosus. The lesions involve the forehead, nose, cheeks and chin, they have a rough, horny feel and are indolent. The second type involves both the flexor and the extensor aspects of the arms. These lesions are dusky red and have violaceous hyperkeratotic and hypertrophic ridges in a coarse reticulated network resembling the pattern seen in striae distensae. The

tops of the ridges have some whitish streaks, which resembles Wickham's striae. The lesions on the arms are somewhat suggestive of hypertrophic lichen planus. The third type of lesion involves the buttocks. It consists in discrete corneous conical papules, like those of advanced keratosis pilaris.

Histopathologic changes in the lesions on the face included hyperkeratosis, follicular plugging and chronic small round cell infiltration of the dermis, most prominent about the appendages of the skin. Biopsy of a specimen from a lesion of the arm showed a lichen-planus-like infiltrate in the upper part of the dermis.

#### DISCUSSION

DR A. E. INGELS: I should like to emphasize the great similarity of these lesions to those of lichen planus histopathologically. It struck me as a possibility that the mechanical quality of the skin proper may invite this particular form of lichen planus, as it sometimes develops in discrete nodes.

DR H. V. ALLINGTON, Oakland: The lesions are most evident on the areas exposed to light. The patient gives a history of flushing easily. She covers the skin from sunlight. Might there not be some factors of photosensitivity in the origin of this eruption?

DR W. M. MEININGER: When the patient was a little girl, she noticed that when she was exposed to light her face would flush. In her mind that was the beginning of her present trouble.

DR HIRAM E. MILLER: The unusual appearance of the lesions in this patient has been of much interest to me. Nekam (*Prasse med* 46:1000 [June 25] 1938) described the findings in a patient with a similar eruption. The lesions on the face and the extremities and the microscopic observations in his patient and in this one are so similar and so unusual that the eruption may be a disease entity. Nekam attempted to separate the disease from the lichens and preferred the name "porokeratosis striata lichenoides" to the term "lichen verrucosus et reticularis" suggested by Kaposi (*Vrhtschr f Dermat* 13:571, 1886) for a somewhat similar eruption. Wise and Rein (*Arch Dermat & Syph* 34:830 [Nov] 1936) described a moniliform type of eruption, which they compared with the eruption described by Kaposi. They also were of the opinion that the term "lichen" was not applicable and suggested the term "morbus moniliformis lichenoides." The appearance of their patient was different from that of Nekam's patient and from that of this patient. In no one of these reported cases do the observations suggest "lichen planus," but in all of them there is recorded a definite lichenoid appearance.

**Ichthyosiform Erythroderma** Presented by DR FRANCES A. TORREY

W. A., a 20 year old white youth born in California, has had a generalized eruption since early infancy. This has become progressively worse since the age of 12. Pruritus has been severe at times.

At present there is an extensive patchy erythematous scaling eruption, which is well defined and symmetrically distributed over the body. The thickened erythem-

atous areas extend to the neck and shoulders, to the flexures of the arms and the legs and over the abdomen. The skin of the back shows thickening and irregular scaling. The greasy scales are most evident in the eyebrows, along the hair line and in the creased areas of the body, where the scales are extremely thick, forming rugae in the cubital fossae. The scalp is free of lesions, but the hair is dry. There is decided perleche. The palms and soles are dry and thickened, with scattered keratotic areas. There are two horns, each 6 to 7 mm in length, on the palmar surface of the left thumb. The nails are misshapen and opaque. There are five teeth missing, and many caries are evident. There is severe photophobia, the lids close to narrowed slits, and there is superficial vascularization of both corneas, with conjunctival irritation. The fundi are poorly seen, but they show no gross abnormalities.

Results of laboratory examinations were as follows: The basal metabolic rate was +15 per cent, the blood cholesterol level was 64 mg per hundred cubic centimeters, the blood count was within normal limits, and the Kahn and Kolmer reactions of the blood were negative. The urine was normal.

There is no history of consanguinity. The seven siblings are all alive and well.

The patient said that he had had a great variety of medication, both oral and topical, without improvement. All lesions are said to have disappeared once for one month, when the patient was in a hospital in Sacramento at the age of 8 years.

On Feb 15, 1944, treatment with 200,000 U. S. P. units of vitamin A daily was started. The patient thinks that there is definite improvement. The photophobia has decreased, and the vision is less "fuzzy." There is no pruritus. The generalized erythema has decreased.

#### DISCUSSION

DR FRANCES A. TORREY: The interesting feature is that the patient apparently is slightly improved since he has been given 200,000 units of vitamin A daily from February 15. His eyes were examined on February 15, by an ophthalmologist, who again saw him yesterday and thought that his eyes were much improved. Up to this time the patient had been progressively growing worse.

DR HARRY ALDERSON: Did he have gonorrhea? Some lesions suggest keratosis blennorrhagica.

DR FRANCES A. TORREY: There is no history of it. He has had this eruption since infancy.

DR HARRY ALDERSON: What preparation of vitamin A has he been taking?

DR FRANCES A. TORREY: The preparation is put up by Gelatine Products, Inc. I am using the capsules containing 25,000 units.

**Histoplasmosis (Darling)** Presented by DR FRANCES M. KEDDIE

D. C., a white man aged 31, was first seen in the dermatologic clinic of the University of California Hospital Dec 8, 1943, because of a history of Hodgkin's disease of five years' duration. At that time he pre-

sented small cervical, axillary and inguinal lymph nodes and an ulcer on the center of the tongue. The ulcer had started about six months before as a small papule, which slowly increased in size and ulcerated in the center. Biopsy of the edge of the ulcer showed endothelial cells filled with small bodies clinically characteristic of *Histoplasma capsulatum*.

A culture of part of the biopsy specimen yielded *H. capsulatum*. Examination of specimens of blood, bone marrow and a lymph node (axillary) showed no

from Jan 28 to Feb 11, 1944, effected no change in the appearance of the ulcer or in the fever.

**A Case for Diagnosis (Pemphigus Vulgaris, Pemphigus Erythematosus [Senear-Usher Syndrome]?)** Presented by DR OTTO E L SCHMIDT

Mrs S H, a 63 year old white American housewife, entered the clinic on Feb 7, 1944, complaining of sores of the mouth and genitalia for sixteen months.

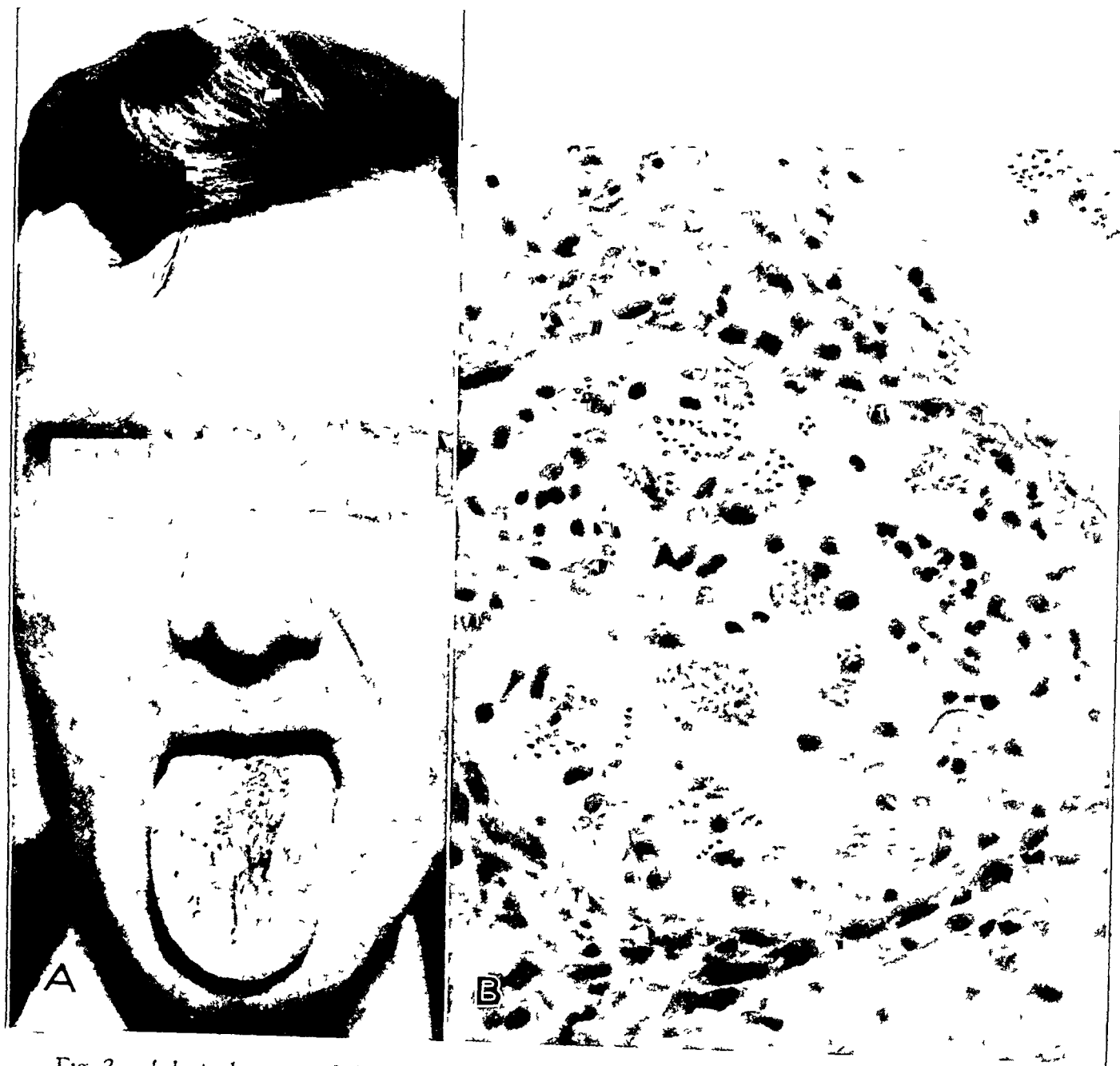


Fig 2—A, histoplasmosis of the tongue and, B, histoplasma capsulatum in a section of the tongue

organisms, either histologically or by culture. The tissue removed in 1938 from the cervical lymph nodes showed, when reviewed, a few cells containing round bodies similar to those seen in the specimen of the tongue.

The serum protein level was 12.07 mg per hundred cubic centimeters (albumin 4.3 mg and globulin 7.77 mg), the calcium level was 8.82 mg, and the phosphorus level was 3.04 mg. The blood count was essentially normal. Roentgen examination of the chest showed no abnormalities. A low grade intermittent fever was present. Sulfadiazine, 6 Gm daily, taken

The past history includes an attack of jaundice twenty-five years ago, an adenoidectomy and a tonsillectomy, performed in 1920 following a peritonsillar abscess, hemorrhoids for the past two years and a "rectocele" for the past nine months.

Sixteen months ago the patient noted a small "sore" inside the lower lip. During the next four months lesions appeared on the entire buccal surface and on the external genitalia. A physician in another city made a diagnosis of "trench mouth" and prescribed a neoarsphenamine mouth wash. The patient stated that she was given weekly treatments of arsenicals intra-

venously and a bismuth preparation intramuscularly for about one year, with little change in her condition. Her diet has consisted entirely of soft and liquid foods. Eight months after the onset of the symptoms, her teeth were extracted, with an ensuing increase in the eruption. For the past six months her eyes have been red and sore, despite local and "electric" treatments by a physician. She has had some epistaxis for three months.

Examination on Feb 7, 1944 revealed a dry crusted lesion, 3 cm in diameter, on the vertex of the scalp. There was trichiasis of both upper eyelids, and the conjunctivas were red and edematous. The choanae were coated with dried blood. There were scattered necrotic ulcers with erythematous borders on the gingivae, and noninflammatory bullae and vesicles were present on the buccal membranes, soft palate and pharynx. Beneath the right breast and in the umbilicus were erythematous indurated lesions, with small peripheral vesicles. In the right inguinal fold were two moist erythematous plaques, 1.5 by 1 cm, which the patient says started as "clear blisters" several months ago. Over the labia minora, the clitoris and for 3 cm into the vagina there were red-bordered ulcerations but no intact bullae. Some external hemorrhoids were eroded. The remainder of the examination revealed no additional abnormalities.

The hemogram showed 3,600 white blood cells, with 38 per cent polymorphonuclear cells, 56 per cent lymphocytes, 2 per cent eosinophils and 4 per cent monocytes. The urine was normal, the serologic reactions were negative. Culture of material from a freshly ruptured vesicle grew nonhemolytic streptococci and staphylococci.

Since admission to the clinic the patient has been given diethylstilbestrol, 1 mg daily for nine days, without results. At present she is taking oral and vaginal washes of 50 per cent solution of zinc peroxide, sitz baths of permanganate, diluted 1:6,000 and the Stuart formula vitamin tablets. She has had the third of weekly vaccinations. The palpebral cilia is being removed in the ophthalmologic clinic.

#### DISCUSSION

DR NORMAN N EPSTEIN: I object to the term "Senear-Usher" for this type of pemphigus, the lesions on the face are much like those of lupus erythematosus lesions, and there are no bullous lesions on the body. If the woman has pemphigus, it is likely that some day she will show a picture of pemphigus erythematosus (Senear-Usher) if she lives long enough.

DR MERLIN T R MAYNARD, San Jose: I agree with the diagnosis of pemphigus and with Dr Epstein, this eruption cannot be diagnosed as Senear-Usher pemphigus.

DR OTTO E L SCHMIDT: The only justification I had for the suggested possibility of its being the Senear-Usher syndrome was that the lesions on the scalp show atrophic changes. Her relatives state that the two plaques she has in the right inguinal fold did start as "blisters," as they put it. Perhaps the lesion on the scalp when cleaned would show more changes resembling lesions of lupus erythematosus. The term "Senear-Usher" was used as a point for discussion. I, too, did not think that this eruption was typical of the syndrome.

## MANHATTAN DERMATOLOGIC SOCIETY

ANTHONY C CIPOLLARO, M D, *President*

WILBERT SACHS, M D, *Secretary*

*April 11, 1944*

### Urticaria Pigmentosa Presented by DR JACK WOLF

W C N, a white boy aged 13 months, is presented with an eruption of ten months' duration, which appeared shortly after vaccination, at the age of 3 months. The eruption was widespread from the beginning, and new lesions have continued to appear. There are no subjective symptoms.

The eruption is profuse, lesions are present on the head and neck, the torso and extremities and the palms and soles. The individual lesion is a small oval-shaped papule, approximately 1 by 0.5 cc, there is little variation as to size and shape. The color is yellowish and suggests the possible diagnosis of xanthoma. On mild friction there is rather pronounced whealing.

#### DISCUSSION

DR FRED WISE: I agree with the diagnosis as presented.

DR WILBERT SACHS: I agree with the diagnosis, but I believe that biopsy of a specimen from a lesion will show an almost pure mast cell infiltration. This type of lesion clinically simulates xanthoma.

DR GIRSCH D ASTRACHAN: I agree with the diagnosis. It is the nodular form of urticaria pigmentosa, which occurs much more rarely than the macular form.

DR THOMAS N GRAHAM: I agree with the diagnosis. This is the nodular type of urticaria pigmentosa, cases of which constitute a small percentage of the total number of cases of this dermatosis.

DR HERMAN SHARLIT: Dr Sachs mentioned a xanthoma-like lesion. These lesions do not look like xanthoma to me, they are much too red.

DR WILBERT SACHS: With an ordinary hematoxylin and eosin stain the pathologic picture sometimes suggests mycosis fungoides, but when stained with methylene blue the growth is shown to be composed entirely of mast cells.

DR JACK WOLF: In daylight these lesions look distinctly yellow and at first sight suggest xanthoma, but an experience with 1 case of xanthoma excludes that possibility immediately, no other diagnosis than urticaria pigmentosa can be entertained. I did not mean to imply that there was a definite relationship between vaccination and the appearance of urticaria pigmentosa. However, it is a fact that numerous cases have been reported in which lesions of this type have appeared after vaccination. Oimsby refers to it in his book.

### Inoculation Tuberculosis Presented by DR ISADORE ROSEN

J E B, a boy aged 4 years, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 4, 1944, with a lesion on the left cheek of seven weeks' duration and left cervical, submaxillary and postauricular adenopathy of four weeks' duration.

Except for a fall against a radiator in October 1943, in which the left side of the face was hit, without evidence of any external injury, the history of the

boy was essentially noncontributory. The parents stated that seven weeks previously a few tiny papular lesions appeared on the left cheek, gradually coalescing to form an erythematous plaque. Four weeks ago lymph nodes below the left jaw and behind the left ear appeared and gradually became larger.

On the left cheek there is an erythematous plaque the size of a nickel, composed of pinhead-sized crusted papules. The plaque is somewhat infiltrated. Below the left jaw anteriorly and posterior to the ear, there are a few hazelnut-sized nodes, some of which are erythematous and about to break open.

General examination in the pediatric clinic revealed nothing abnormal except for the cutaneous lesion and the adenopathy. A roentgenogram of the chest showed no abnormalities. A blood count on April 3 revealed a moderate leukocytosis (12,450 leukocytes) and a relative lymphocytosis (50 per cent large lymphocytes, 3 per cent small lymphocytes, 3 per cent monocytes, 1 per cent eosinophils, 5 per cent basophils and 38 per cent polymorphonuclear leukocytes).

Tuberculin in a dilution of 1:5,000 and a tuberculin patch test elicited negative reactions.

#### DISCUSSION

DR MAURICE J COSTELLO I agree with the diagnosis of inoculation tuberculosis, but I should expect the patient to have a positive reaction to an intradermal tuberculin test by this time, because of the extension of the disease process to the cervical lymph nodes.

DR GEORGE M LEWIS Clinically this case does not resemble those of inoculation tuberculosis I have encountered, in which there have been subcutaneous, nodular lesions. There is more resemblance in this case to a superficial fungous infection. The absence of a positive reaction to tuberculin and of contact with tuberculosis are further reasons to doubt Dr Rosen's diagnosis.

DR GIRSCH D ASTRACHAN I believe that this is probably a case of primary tuberculosis, although I feel, as Dr Lewis does, that a fungous infection should be ruled out.

DR FRED WISE I am inclined to agree with Dr Lewis' statement, at least to the extent of saying that more proof is necessary before making a diagnosis in a case of this kind. The lesion does not resemble the customary ones of inoculation tuberculosis, and, if it were not for the history of seven weeks' duration, I should offer a diagnosis of herpes facialis.

DR HERMAN SHARLIT I, too, am impressed by the superficial character of this lesion and feel the need for more evidence before accepting a diagnosis of primary tuberculosis of the skin.

DR E WILLIAM ABRAMOWITZ Of course, the full evidence for primary inoculation tuberculosis is not in. It is not necessary to have an ulcerative lesion, although it is common. This is a favored location for primary inoculation tuberculosis. I am not acquainted with any swelling of the lymph nodes in this manner that occur in fungous infections. A duration of four or five weeks practically excludes herpes of any kind. A dark field examination has not been performed in this case, but the Wassermann reaction of the blood was negative. One can explain the negative reaction to tuberculin by the possibility that the tuberculin used was not fresh. Results of roentgenologic examination of the lungs were reported as negative for tuberculosis. One hesitates to traumatize the lesion, even to obtain a specimen for biopsy. Some physicians state that if such lesions are left strictly alone they will heal. A smear has been made from one of the abscessed nodes and some material also has been inoculated into a guinea pig.

DR FRED WISE Would material from a puncture of the lymph nodes behind the ear show tubercle bacilli if the lesion is one of inoculation tuberculosis?

DR E WILLIAM ABRAMOWITZ It might, and it might not.

DR FRED WISE Scarification of a rabbit's cornea with fluid from the lesion would possibly determine the presence of herpes.

DR MAURICE J COSTELLO May I suggest that a smear be made of the discharge from the fluctuant area behind the ear and examined for tubercle bacilli? I should not incise this lesion.

DR ANTHONY C CIPOLLARO I saw this patient when he first came to the clinic. My impression at that time was that he had either inoculation tuberculosis or lupus vulgaris. The possibility of his having a fungous infection or herpes also entered my mind. I think that it is difficult to make an unequivocal diagnosis of primary tuberculosis. It is impossible in some instances to fulfil all the criteria required for the diagnosis of inoculation tuberculosis: a negative tuberculin reaction prior to inoculation and the development of a nodular ulcerative lesion accompanied with malaise and elevation of the temperature, to be followed after the appearance of the lesion by a positive tuberculin reaction. My impression tonight, after all the discussion, still is that one is dealing here with primary tuberculosis. It will require further observation and tests before one can arrive at any definite conclusion.

DR ISADORE ROSEN Most of the questions raised by the discussers were answered by Dr Abramowitz and Dr Cipollaro. The patient has been under observation for only a short time, and not all tests have been completed. It is not necessary for primary inoculation tuberculosis to be chancreiform in character, it may appear in a variety of forms. The possibility that this is a fungous infection should be taken into consideration, although I have never seen that type of infection produce symptoms such as are present in this instance.

#### A Case for Diagnosis (Periphlebitis, Perivasculitis Nodularis Necrotisans. Erythema Induratum of Unusual Type?) Presented by DR MAURICE J COSTELLO

F T, a married Italian woman aged 43, with five children, has had an eruption on her legs since she began to work as a sewing machine operator in a dress factory, a year and a half ago.

Her father died of diabetes. Her husband had syphilis many years ago, but the patient was not infected, and the Wassermann reaction of her blood is negative.

The eruption consists of a number of somewhat painful indurated scaly lesions, ranging from a half-dime to a silver dollar in size. A number of the lesions have broken down, revealing a punched-out opening with a grayish discharging base, measuring about 5 mm in diameter. There are more lesions on the left leg than on the right.

A roentgenogram of the lungs gave no evidence of pulmonary tuberculosis. A Vollmer patch test and an intradermal test with tuberculin, diluted 1:1,000, were performed yesterday. The Wassermann reaction of the blood is negative, and the urine is normal.

#### DISCUSSION

DR GEORGE M LEWIS I think that a diagnosis of erythema induratum is tenable. Trauma may be a precipitating cause.

DR THOMAS N GRAHAM I favor a diagnosis of erythema induratum, in spite of the location of some

of the lesions on the extensor surfaces of the legs. The lesions themselves are typical of this dermatosis.

DR GIRSCH D ASTRACHAN I also think that this is Bazin's disease (erythema induratum), in spite of the fact that some of the lesions are very painful. I have seen lesions of that kind in erythema induratum.

DR WILBERT SACHS I believe that the lesions presented by the patient would justify either diagnosis. She is not too old to have erythema induratum and not too young for a periphlebitis. Some lesions are painful and some are not. I think that one cannot differentiate clinically between the two diseases at this time, and biopsy may be of help. If one finds changes in the deep vessels and tubercles about them, one may be able to say that this is the tuberculous type of perivasculitis.

DR ISADORE ROSEN Time and again one sees patients with lesions similar to those present in this patient. Some of the ulcers are superficial, others, again, are fairly deep. They may be associated with the ingestion of drugs or other toxic substances. They would hardly fit in with the classic manifestations of erythema induratum, owing to the location, the superficial character of the lesions and the age of the patient, the lesions do not conform to this disease.

DR HERMAN SHARLIT I am prepared to accept both diagnoses. I am impressed with the fact that the trouble occurs predominantly in women. I wonder whether any one has ever studied its relation to pregnancy and whether these patients have had phlebitis or any other disease peculiar to women that may have been a predisposing cause.

DR MAURICE J COSTELLO Clinically, at first sight, one might make a diagnosis of erythema induratum, but if that diagnosis were made, one would have to say that it is of an unusual type. Lesions of erythema induratum as a rule are deeper and less painful than these. The patient never had lesions on the legs until two years ago, when she began to work. In regard to Dr Sharlit's observation, I think it is a disease occurring almost exclusively in women. Dr Bechet wrote a paper in which he said that periphlebitis nodularis necroticans is identical with erythema induratum.

#### A Case for Diagnosis (Vasculitis, Periarteritis Nodosa?) Presented by DR E WILLIAM ABRAMOWITZ

R B, a woman aged 46, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in March 1944, complaining of an eruption on her legs of five months' duration. According to her history, painful dark bluish spots have been recurring from time to time, some of which have broken down after days or weeks. The patient gives a history of having taken large quantities of acetylsalicylic acid. General examination revealed nothing abnormal.

On the lower third of the legs anteriorly and to a lesser degree posteriorly there is a moderate number of nickel-sized and somewhat larger blackish-bluish round macules and ulcers.

The urine was normal. The Wassermann reaction of the blood was negative. Hematologic examination showed 3,930,000 erythrocytes, 66 per cent hemoglobin, 280,000 platelets, 11,050 leukocytes, with a normal differential count, bleeding time of three minutes forty-nine seconds, coagulation time of twenty-five minutes and normal clot retraction and fragility.

Histologic examination of a lesion showed vasculitis and perivasculitis.

#### DISCUSSION

DR HERMAN SHARLIT Certainly this patient's ingestion of iodides has been constant, and it would be a sensible move to stop it and see what happens.

DR WILBERT SACHS In the section there were changes in the vessels and about the vessels. For a diagnosis of vasculitis, there must be damage to the vessels. I suggested a cardiovascular examination, and I still feel that the patient may have some associated vascular disease.

DR ISADORE ROSEN I saw this patient on her first admission to the clinic, and the lesions were erythematous and bullous, with superficial erosions, giving the picture of bullous erythema multiforme. As the patient had been taking many types of medicines, I associated the eruption with the ingestion of drugs.

DR ANTHONY C CIPOLLARO My impression is that this is not a disease of the erythema induratum type but one due to ingestion of a drug.

DR E WILLIAM ABRAMOWITZ The names "vasculitis" or "perivasculitis" do not seem to help us or the patient. It is important to keep such patients off their feet, even those with Bazin's disease (erythema induratum). When they fail to respond to other kinds of treatment, they will improve when kept off their feet.

#### Purpura of Unknown Cause Presented by DR THOMAS N GRAHAM

M K, a white girl aged 17, was first seen at the New York Hospital on March 15, 1944, complaining of an eruption of two and a half months' duration, involving the extremities, buttocks and abdomen. It first appeared on the medial aspect of each thigh just above the knee and gradually spread to its present distribution. During a period of three and a half weeks' observation a number of new lesions appeared. There have been no subjective symptoms.

There is no history of ingestion of drugs except for acetylsalicylic acid taken not oftener than once every two or three months. There is no history of allergy or arthritis. The tonsils have been removed, and the patient is not subject to attacks of pharyngitis. The teeth have recently been treated, and they show no evidence of infection. Her diet has been adequate and has not been lacking in vitamin C.

There are numerous discrete and confluent petechiae, most pronounced on the legs, thighs and buttocks. On the lateral aspect of the thighs and on the buttocks, in addition to the petechial lesions, are irregular erythematous scaly patches. There are several areas on the legs in which the arrangement of the lesions suggests an annular configuration. There is no atrophy of the involved cutaneous areas.

A Rumpel-Leede test, with a pressure of 100 mm of mercury for ten minutes, resulted in the appearance of ten purpuric spots.

The blood count was as follows: hemoglobin, 11.9 Gm, red blood cells, 4,200,000, platelets, 180,000, white blood cells, 8,000, with lymphocytes, 48 per cent, polymorphonuclear leukocytes, 47 per cent, mature cells, 7 per cent, monocytes, 6 per cent, eosinophils, 1 per cent, and basophils, 1 per cent. Clotting time of the blood was five and a half minutes, and bleeding time was thirteen minutes. The Cair sedimentation index was 0.25, the total fall, 10 mm, and the red blood cell value, 43 per cent.

A Mazzini reaction of the blood was negative.



## DISCUSSION

DR FRED WISE Dr Rosen's suggestion of parapsoriasis is well considered, because several cases of parapsoriasis guttata with hemorrhagic lesions have been described in the literature. But undoubtedly the presence of annular lesions, of which I saw two clearly, must make one think of Majocchi's disease (purpura annularis telangiectodes). This disease presents a great many different individual lesions and is described as manifesting different morphologic characteristics, although I should not venture a diagnosis of purpura annularis telangiectodes, I think that it should be borne in mind. One of the peculiarities of this disease as contrasted with ordinary purpura is that in purpura annularis telangiectodes there are as a rule no metabolic disturbances of serious nature. Once in a while the patients complain of arthritis, but there are no changes in the blood picture. This patient seems to have no detectable lesions aside from those of the skin.

DR E WILLIAM ABRAMOWITZ In the absence of any abnormal laboratory findings, I think that this is probably a case of what is called purpura simplex, in many cases of which one cannot find a cause. It may help to estimate the vitamin C content in the blood, in spite of the fact that the patient is supposed to have an adequate diet. I attach little importance to ringed lesions on the legs, because I have found them in several types of eruptions.

DR JACK WOLF The lesions on the arms are suggestive of parapsoriasis, and the lesions on the lower extremities are definitely those of purpura. In the absence of scaling on the forearms, I should be inclined to classify the lesions there as part of the picture of purpura rather than of parapsoriasis, since they are also more edematous than lesions of classic parapsoriasis.

DR GEORGE M LEWIS The classification of purpura seems unsatisfactory, and one seldom determines the cause. Perhaps a platelet count to rule out thrombopenia is the most important laboratory procedure in all cases of purpura. The duration of the lesions in this case is long for ordinary purpura, since in the majority of cases lesions subside in a few weeks. This patient still has active lesions after three and a half months. The presence of annular lesions is of interest.

DR GILKES D ASTRACHAN I think that this is some kind of a toxic eruption, and I suggest a study of the blood chemistry for urea nitrogen, uric acid and the icterus index. Also, I suggest the making of a platelet count. I agree with Dr Rosen that the lesions of the upper extremities strongly suggest parapsoriasis.

DR WILBERT SACHS I believe that the patient has purpura simplex, and for this disease one does not find the cause. If there were any other features, it would not be purpura simplex.

DR THOMAS N GRAHAM Biopsy of sections from the lesions should show whether this patient has either parapsoriasis or purpura annularis telangiectodes. With regard to Dr Abramowitz' suggestion that exposure to chemicals may have caused the eruption, the patient stated that she had used a henna preparation on her hair a number of times. I did not consider this information important, because there was no evidence of local cutaneous sensitization.

NOTE.—Observations on biopsy were consistent with a diagnosis of purpura and ruled out parapsoriasis and purpura annularis telangiectodes (Majocchi).

# A Case for Diagnosis (Ichthyosis, Lichen Planus Hypertrophicus?) Presented by DR MAURICE J COSTELLO

R A, a woman aged 45, was born in Colombia, South America, where she resided until several months ago. An eruption has been present for the past twelve years, although the patient's skin has been dry most of her life. Severe pruritus has been a prominent feature recently. The eruption, which is well demarcated, involves the extremities chiefly, the skin of which is hyperpigmented, lichenified and covered with scratch marks. There are a number of discrete slightly elevated violaceous pruritic lesions, the size of a pea, some of which have a verrucous surface on the extremities.

Biopsy of one of these lesions, by Dr Sachs, showed that the epidermis was not acanthotic or thin. The surface was verrucous and covered by an increased loosely laminated horny layer. There was a tremendous amount of pigment in the basal cell margin. The elastic tissue was fragmented but present. It was felt that the lack of reaction and the presence of elastic tissue ruled out acrodermatitis chronica atrophicans and that there were no pathologic features that would fit in with lichen planus.

There is thinning of the skin on the backs of the hands but no atrophy of the interosseous muscles. There is some impairment of the sensation of touch but none of heat and cold.

The Wassermann reaction of the blood was negative. Examination of nasal smears for *Mycobacterium leprae* was unsuccessful on two occasions.

Treatment has consisted of small doses of thyroid extract and 150,000 U S P units of vitamin A taken daily, with local administration of bland lubricating oils.

## DISCUSSION

DR FRED WISE Leprosy seems to me to be the most probable diagnosis.

DR HERMAN SHARLIT I cannot say that I am not impressed by these judgments, but I still think that the patient is a victim of her place of origin. If she did not come from where she does, I should not think of leprosy. She has been given a great deal of arsenic.

DR E WILLIAM ABRAMOWITZ The pigmentation stops sharply at the thighs, and then there are little elevated almost keratotic lesions on the thighs, which I thought at first might be due to arsenic. There were none on the body. I believe that leprosy must be ruled out.

DR GEORGE M LEWIS In early leprosy the symptoms and signs may be minimal, and I should favor that diagnosis.

DR WILBERT SACHS The total lack of inflammatory process in the cutis is against a suggestion of leprosy. However, I shall stain for the organism. If there are no organisms, and with the absence of *lepra bacilli* in the nasal smears, I think that leprosy can be ruled out.

DR MAURICE J COSTELLO This patient saw a number of physicians in Bogota, Colombia, several of whom were dermatologists, and she stated that each one made a different diagnosis. When I first saw her my initial thought was of leprosy because of her place of origin, the sarcoid-like lesion and other indications. She has no loss of sensation to heat or cold, but there is some loss of sensation to touch. I tried the histamine test, and the result was negative. This patient came to me for relief of severe itching which I have known to occur on occasion in patients with leprosy. She presented an eruption that looked like neuroderma-

titis because of the severe pruritis. The nasal smears did not show *Mycobacterium leprae*. I cannot understand why a lesion of this type, which suggests lichen planus hypertrophicus clinically, does not show something suggestive of that dermatosis histologically.

**Tuberculosis Verrucosa Cutis in a Patient with Advanced Pulmonary Tuberculosis** Presented by DR MAURICE J COSTELLO

J McC, a white man aged 56 from St Joseph's Hospital for Chest Diseases, has had two lesions, one on the back of each hand, for the past year. The lesion on the left hand has healed, leaving a hyperpigmented and depigmented half-dime-sized scar. That on the right hand is about nickel-sized and is divided into three zones, with a well marked border, which is erythematous. The central portion is papillomatous, with secondary infection.

Three hundred roentgens were applied to the active lesion on March 18, 1944.

DISCUSSION

DR GEORGE M LEWIS. The spontaneous disappearance of one of the lesions is interesting.

DR GIRSCH D ASTRACHAN. Several months ago I saw a patient with two ulcerations, one on the forehead and the other on the hand, in the tuberculosis ward of the Metropolitan Hospital. Biopsy, made in Bellevue Hospital, of a section from the lesion on the forehead proved the ulceration to be caused by tuberculosis. However, the smear for *Mycobacterium tuberculosis* was negative. The lesions were resistant to therapy. One ulceration improved rather rapidly, however, when a sulfanilamide ointment was applied. How can one explain the appearance of the ulcers in these areas? As is known, tuberculous ulcerations usually appear around the mucotaneous openings.

DR HERMAN SHARLIT. Is it not unusual for tuberculosis of the skin—or any other kind—to get well spontaneously?

DR MAX SCHEER. It is not unusual for tuberculosis of the skin to heal spontaneously.

DR MAURICE J COSTELLO. I have seen several patients with tuberculosis verrucosa cutis coexisting with pulmonary tuberculosis. It occasionally occurs in orderlies working in institutions caring for tuberculous patients. I have seen tuberculous gummas on the skin that looked just like those described by Dr Astrachan. They may occur spontaneously, without an underlying tuberculous focus in the bones or joints. I have known these lesions to occur in patients with scrofuloderma but in locations not overlying tuberculous foci.

**NEW ENGLAND DERMATOLOGICAL SOCIETY**

JACOB H SWARTZ, M D, *President*

FRANCIS M THURMON, M D, *Secretary*

*April 12, 1944*

**Pityriasis Lichenoides et Varioliformis Acuta** Presented by DR J HARPER BLAISDELL, Boston

Mrs H, a 27 year old white woman, presents a fairly generalized eruption of five weeks' duration.

Her past history revealed an attack of urticaria ten years previously, and since that time there has been a

symptomless dermatographia. She has been married for five years. She has a boy 3 years old, and on Feb 8, 1944 she delivered a second child, who is normal in all respects. There have been no miscarriages. The Hinton reaction of the blood during pregnancy was negative.

The present illness began five weeks ago, when the patient noticed an oval lesion, 3 cm in diameter, on the right lower portion of the trunk. Seven days later the present eruption appeared on the arms. Ten days later she had a sore throat. When the patient was first examined two weeks ago, there was generally distributed over the anterior portion of the trunk, the thighs and particularly the upper extremities a dull red maculopapular and papular eruption, the lesions of which ranged from a pinhead to a pea in size. Only an occasional lesion was present on the face. A few lesions were crusted, an occasional one was pustular, and two of the pustules showed umbilication. Four days later the eruption had increased 50 per cent. The trunk, especially the back, was generally affected. The lesions subject to friction became crusted.

At present there is a further extension of the eruption. A few of the older areas have flattened and now are represented merely by pigmentation. Crusting is more prominent than before. Some of the papules are surmounted by vesicopustules, no umbilication is present.

DISCUSSION

DR ALBERT LEVENSON, Bridgeport, Conn. I favor the diagnosis of parapsoriasis varioliformis acuta (Haberman type). The patient presents a multiform eruption, which consists of papules, vesicles, vesicopustules and crusts. The eruption seems not to have the characteristics or distribution of secondary syphilis. Also there are no palmar or plantar lesions demonstrable.

DR WALTER F LEVER, Boston. The eruption is like a textbook picture of parapsoriasis of the varioliform type.

DR MAURICE J STRAUSS, New Haven, Conn. Dr Blaisdell tells me that the result of the second serologic test for syphilis has not been reported. I feel sure that it will be negative.

DR ELLWOOD C WEISE, Bridgeport, Conn. I still prefer to adhere to the diagnosis of pityriasis lichenoides et varioliformis acuta of Haberman.

DR BERNARD APPEL, Lynn, Mass. There is practically unanimous agreement in the diagnosis. I should like only to question the terminology. It seems to me that one contribution which we can make in our meetings toward the clarification of the problems of dermatology is to straighten out the nomenclature. I tried, when calling this meeting together, to emphasize to those dermatologists who represented the different clinics the importance of adhering to the terms for diseases as they are presented in the "Standard Nomenclature of Disease and Standard Nomenclature of Operations." This case represents a good example of the necessity of standardizing the nomenclature. There have been three diagnoses. The first was parapsoriasis varioliformis, the second was parapsoriasis lichenoides, and the third was pityriasis lichenoides et varioliformis acuta. The last term is the only one officially recognized in the "Standard Nomenclature." The disease was first described by Haberman and Mucha, and the manifestations in this case clearly fit that description. I remember the first case of this disease presented before this Society, a number of years ago, in which the same problem of differentiation from secondary syphilis arose.

DR JOHN G DOWNING, Boston I should like to agree with Dr Appel about the use of correct terminology. When I see a vesicular eruption which is labeled syphilis, I am still old fashioned enough to disregard that diagnosis. On the medial aspect of the patient's left foot there is a vesicle, slightly milky in color, with a definite areola of erythema. I favor the diagnosis of *pityriasis lichenoides et varioliformis acuta*.

DR JACOB H SWARTZ, Boston I believe that the subject of vesicular syphilis is important. I remember a case presented at the Massachusetts General Hospital when I had just finished studying exanthematous diseases in the South Department of the Boston City Hospital. I called the disease variola, but it later turned out to be a varioliform syphilid.

DR OSCAR R JOHNSON, Portland, Maine I am wondering about the serologic reaction. Has a titration of the serum been done?

DR J HARPER BLAISDELL, Boston This woman presented herself at my office two weeks ago. She was in tears because the diagnosis of syphilis had been suggested. Ten weeks ago, at the time of her delivery, she had a negative Hinton reaction of the blood. Two weeks following delivery, she noticed a lesion on the lateral abdominal wall which did not trouble her. Ten days later she noticed the present lesions, which were a little different when I saw her two weeks ago than they are today. The eruption is more papular and duskier today than it was at that time. The patient had several lesions, perhaps three or four, which were varioliform in type. During the past two weeks the friction from clothes easily traumatized the top of the papules, and crusting occurred. On the foot today a papule is surmounted by a vesicopustule. There have been no palpable lymph nodes. Three weeks ago the patient gave a history of a sore throat, but there were no mucous patches. At the time of my original examination I considered the diagnosis of secondary syphilis. The more I observed the eruption, the more uncertain I was. Dr Swartz looked at it and suggested that it might be the varioliform type of parapsoriasis. Dr Lee McCarthy, of Washington, has discussed the varioliform type of parapsoriasis in Wise and Sulzberger's 1942 Year Book of Dermatology and Syphilology. Scaling plaques are typical of this syndrome, this woman has none. If the eruption is pityriasis of the varioliform type, one can assume that the lesion on the abdominal wall was the "herald spot." Two weeks ago the rapid Hinton reaction of the blood was negative, and a week ago the Wasserman, Kahn and Hinton reactions were negative.

**A Case for Diagnosis (Neurotic Excoriations, Dermatitis Factitia?)** Presented by DR JOHN ADAMS, Boston

A G, an Italian laborer aged 55, presents an eruption on the face and neck of three years' duration.

The primary lesion, a papule, developed on the left nasolabial fold and formed an ulceration. From this site it extended to the adjacent portion of the upper lip. A yellowish crust formed over this area, accompanied with intense burning and itching. A year later similar lesions developed on the left side of the neck. They were sharply defined irregular ulcers, one of these measured 4 cm in diameter and had an erythematous base with a granulomatous glistening surface, which secreted serum. At the same time a macular lesion, 11 cm in diameter, appeared on the medial surface of the left thigh. During the course of the past year these lesions gradually disappeared,

while new lesions developed on the right cheek, the forehead and the left side of the neck. During a recent period of hospitalization the patient gave a definite history of having deliberately gouged his face, because, as he stated, "there is something in there, and I have to get at it."

On the right cheek and the left side of the neck there are irregular crusted lesions, semirectangular in shape, with linear streaks radiating toward the nose and chin.

Biopsy of an ulceration on the cheek six months ago revealed "chronic inflammation." Serologic reactions for syphilis were repeatedly negative.

At weekly intervals for two months prior to Dec 3, 1943, roentgen therapy was administered, a total of 780 r to the right side of the face and left side of the neck and 420 r to the middle third of the face. After this the patient was hospitalized. Treatment with boric acid ointment resulted in practically complete involution of the lesions by the tenth hospital day.

DISCUSSION

DR G MARSHALL CRAWFORD, Brookline, Mass At one time I considered a diagnosis of dermatitis factitia. One morning it was pointedly suggested within the patient's hearing that he should have lesions on the back of his neck. The next week he had them.

DR WALTER F LEVER, Boston I favor the diagnosis of neurotic excoriations. There is no difficulty in getting the patient to admit that he digs the lesions. I followed his progress in the outpatient department before he received roentgen ray therapy. I asked him several times whether he dug at the lesions and he admitted that he did—he just could not help it.

NOTE—A subsequent report from Dr Joseph Goodman indicates a diagnosis of tertiary cutaneous syphilis. He obtained a history of a penile lesion twenty-seven years ago, treated at a drugstore by local application. Physical examination revealed enlargement of the head of one clavicle. Additional blood tests for syphilis have produced negative reactions. A roentgenogram of the cardiac stripe revealed enlargement of the ascending aorta. The cerebrospinal fluid was normal. Oral administration of potassium iodide for two weeks was followed by remarkable improvement. The lesions have continued to regress with routine chemotherapy for syphilis.

**Pityriasis Rubra Pilaris** Presented by DR GEORGE SCHWARTZ, Malden, Mass

Mrs G, a housewife aged 46, noticed dry red scaling oblique areas on the scalp, face, chest and back six months ago.

Within three weeks, this eruption became generalized and pruritus was severe. The skin was deep red and infiltrated and was covered with fine scales. There was generalized adenopathy and loss of hair from the scalp, axillas and pubic regions. The hands and feet were swollen, and a brief and partial loss of sensation in the finger tips and toes was noted. The palms and soles were indurated. The patient experienced constant sensations of chilliness. No history of medication preceding this eruption could be elicited.

Examination reveals a superficial hyperemia of the entire integument. Small laminated, branlike scales are profuse. Large plaques of scarring are present on the palms and soles. The nails are friable, thickened and yellowish and have lost their luster. There is considerable loss of hair from the scalp, axillas and pubic regions.

The Hinton reaction of the blood was negative. Cultures of clippings from the nails were negative for fungi.

Small doses of roentgen rays at weekly intervals have relieved the pruritus.

#### DISCUSSION

DR FRANCIS M THURMON, Boston. I believe that this case can be classified as a case of lymphomas and will prove to be a case of either leukemia or mycosis fungoides. An occasional case of generalized psoriasis has been observed in which the eruption started as seborrheic dermatitis of the scalp.

DR WILLIAM R HILL JR, Boston. The observations at biopsy were consistent with psoriasis.

DR E MYLES STANDISH, Hartford, Conn. I think that the lesions of the soles and palms are consistent with psoriasis. My diagnosis is erythroderma psoriaticum.

DR JACOB H SWARTZ, Boston. I recall similar cases at the Beth Israel Hospital in which the observations of a pathologic examination were consistent with psoriasis. One case was that of a young girl, and the other, of a middle-aged woman. It turned out that both had pityriasis rubra pilaris. The large follicular openings and the plugging of the dorsal phalangeal areas, together with keratosis, are typical of pityriasis rubra pilaris.

DR JOHN G DOWNING, Boston. There is one addition I should like to make to Dr Swartz's observation: the peculiar yellowish appearance, especially of the palms, and the scaling on the elbows and the wrists. I thought this was a typical picture of pityriasis rubra pilaris.

DR BERNARD APPEL, Lynn, Mass. I agree with the diagnosis as presented. According to the patient's history, the eruption resembled a seborrheic dermatitis or psoriasis at the onset. Many such eruptions are diagnosed as one or the other of these entities before the development of palmar and plantar hyperkeratosis and the subsequent follicular keratotic plugging, such as occurred in this case.

#### A Case for Diagnosis (Neurodermatitis Circumscripta, Dermatitis Factitia?) Presented by DR GEORGE E MORRIS, Boston

G L, a white American girl aged 14, presents a lesion on the proximal phalanx of the right index finger of three years' duration.

At the onset there was a small elevated area, which gradually enlarged. There is no history of medication or trauma.

Examination shows an elevated thickened infiltrated area, 1.2 cm in diameter, on the dorsal surface of the proximal phalanx of the right index finger. On palpation it feels rough and leathery. Pressure produced no change in the lesion.

The Hinton reaction of the blood was negative.

No improvement was noted after the use of occlusive dressings for a period of two weeks.

#### DISCUSSION

DR ELLWOOD C WEISE, Bridgeport, Conn. I should like to support the diagnosis of dermatitis factitia. The child is righthanded and can easily bring her right hand up to her mouth. I think that she produces trauma by sucking the dorsum of the proximal phalanx.

DR FRANCESCO RONCHESE, Providence, R I. The girl bites her finger nails severely. In spite of her denial, I believe that the lesion on the index finger is self-inflicted. This practice is not as common as

nail biting. It is often unrecognized, and the resulting lesions have been diagnosed as warts, dermatophytosis or keloids.

DR WILLIAM B COHEN, Providence, R I. It was stated in the history that this lesion was covered with an occlusive dressing for two weeks, with no resulting improvement.

DR ELLWOOD C WEISE, Bridgeport, Conn. I still support my original diagnosis. Two weeks was not a sufficiently long trial of occlusive dressings. A plaster of paris cast on her finger for a longer period might give results.

DR FRANCIS M THURMON, Boston. I suggest the diagnosis of nevus. I have seen a similar nevus in a girl 13 years old, which had been present since birth.

DR JOSEPH GOODMAN, Boston. I was about to offer the diagnosis of nevus or sarcoid. It would be of interest to have a biopsy.

DR JACOB H SWARTZ, Boston. I should like to add the diagnosis of granuloma annulare. When the lesion is stretched, the waxy, hard border suggests granuloma annulare.

DR E MYLES STANDISH, Hartford, Conn. It seemed a little soft for granuloma annulare.

#### A Case for Diagnosis (Lupus Vulgaris, Sarcoid [Darier-Roussy]?) Presented by DR LEO KORETSKY, Chelsea, Mass

J S, a white American school boy aged 6, presents a lesion on the left cheek of four months' duration.

The area has remained discrete and has not increased in size.

On the left cheek the patient presents a raised irregular plaque, 2 cm in diameter. Its surface is red and is studded with discrete papules, gaping follicles and pustules.

Local applications of sulfathiazole ointment and an ointment of sulfur and salicylic acid together with ultraviolet irradiation have produced no benefit.

#### DISCUSSION

DR JOHN G DOWNING, Boston. I suggest a diagnosis of lupus vulgaris.

DR WILLIAM R HILL JR, Boston. I believe that this is primary inoculation tuberculosis. The child has a lesion on the face and the left cheek, and the regional lymph nodes are palpable. I think that this lesion will heal and these nodes will break down.

DR J HARPER BIAISDELL, Boston. What treatment is proposed in this case?

DR JOHN G DOWNING, Boston. Forty per cent mercuric nitrate ointment topically applied, should be beneficial. I think that this is not primary inoculation tuberculosis.

DR FRANCIS P MCCARTHY, Boston. I think that this is not primary inoculation tuberculosis. I suggest the use of solid carbon dioxide on the basis of the possible diagnosis of lupus vulgaris.

DR WALTER F LEVER, Boston. I believe that this is lupus vulgaris rather than primary inoculation tuberculosis. I suggest excision of the lesion followed by skin graft. If not treated quickly enough, a lesion of this type may enlarge.

DR G MARSHALL CRAWFORD, Brookline, Mass. I should like to emphasize Dr Lever's statements. For lupus vulgaris this is rapid development to occur in four months, but I think that such is probably the diagnosis. When lupus progresses as rapidly as that

all the ordinary destructive measures would simply serve to extend the disease. I have seen smaller lesions than these result in widespread destruction, even after serious attempts have been made in the use of various caustics. These should be radically excised down to the fascia.

**A Case for Diagnosis (Lichen Planus, Lichenoid Purpuric Dermatitis [Gougerot and Blum], Avitaminosis A, Parapsoriasis?)** Presented by DR JACOB H SWARTZ, Boston

A P, a Russian Jewish housewife aged 46, complained of an eruption over the extensor surfaces of the arms and a small area on the neck, of nine months' duration.

At the onset the lesions on the arms appeared to be "blackheads." Recently these lesions have become more extensive, and itching has been noted.

Examination revealed a reticulated pigmented lichenoid eruption over the upper extremities, most pronounced on the extensor surfaces. Keratosis pilaris was present on the thighs. A small similar area was evident on the neck.

Biopsy was inconclusive. Results of six serologic examination of the blood were reported as follows: the Hinton reaction positive, the Hinton reaction doubtful and the Hinton and the Wassermann reactions each negative twice.

There has been no treatment.

#### DISCUSSION

DR JOHN G DOWNING, Boston. In spite of all those suggested diagnoses, I have the temerity to present my usual diagnosis of contact dermatitis. This woman is a stitcher, working with many kinds of cloth. She stitches artificial leather, with which her arms come in contact. I inquired about her clothing. She wears a thin cotton dress, and dust could sift down onto her thighs.

DR GEORGE E MORRIS, Boston. In a study of lichen planus folliculosis circumscriptus (Combes, F C, and Bluefarb S M. *ARCH DERMAT & SYPH* 44:46 [July] 1941) lesions similar to those present in this patient have been described. I suggest this diagnosis in the present case.

DR G MARSHALL CRAWFORD, Brookline, Mass. Dr Downing's diagnosis of contact dermatitis seems likely. This woman cleans her stitching machine fifteen or twenty times a day with kerosene, followed by an oil. That would present the possibility of an oil dermatitis.

DR JACOB H SWARTZ, Boston. The fact that I have offered a variety of diagnoses admits my inability to be positive. The only reason I thought of lichenoid purpuric dermatitis was because of the hemorrhagic reticulated character of the eruption. Diascopy reveals a definite pigmentation. There is an alignment of the lesions which I have not seen in contact dermatitis. I am interested in Dr Morris' diagnosis.

**A Case for Diagnosis (Morphea?)** Presented by DR FRANCIS M THURMON, Boston

M S, a Nova Scotian housewife aged 58, presented a lesion on the left upper quadrant of the abdomen, of twenty-eight years' duration.

The lesion appeared after irritation caused by a corset strap.

Examination reveals an irregular rectangular atrophic area, 18 cm by 15 cm in its greatest transverse diameters.

The Hinton, Kahn and Wassermann reactions of the blood were negative. Biopsy was not performed.

#### DISCUSSION

DR C GUY LANE, Boston. I feel that this is a basal cell epithelioma of superficial type rather than a morphea. I recommend excision.

DR WILLIAM R HILL JR, Boston. In 1932 this patient took two bottles of a liquid medicine for iritis, the administration of which began with one drop. I propose a diagnosis of arsenical epithelioma.

DR LEON BABALIAN, Portland, Maine. I should like to propose the diagnosis of *epithelioma plan cicatriciel*, as described by French physicians; biopsy should be done.

DR MILDRED L RYAN, Brockton, Mass. This patient told me that a corset steel had irritated the skin. I agree with Dr Lane's diagnosis.

DR FRANCIS M THURMON, Boston. I accept the diagnosis of epithelioma. After biopsy, I shall excise the lesion.

**A Case for Diagnosis (Dermatitis Medicamentosa?)** Presented by DR FRANCIS M THURMON, Boston

H G, an American born Negro woman aged 44, presented a generalized erythematous squamous eruption of five months' duration.

She was being treated for tertiary asymptomatic syphilis, when on Oct 25, 1943, after the seventh treatment with neoarsphenamine (0.6 Gm), itching scaly lesions, resembling pityriasis rosea, developed on the trunk. On November 26 lesions resembling mucous patches were observed on the lips, tongue, buccal mucosa and uvula. A moist excoriated papule was observed on a labium. These mucosal lesions cleared by November 29, but the cutaneous eruption persisted and continued to spread, involving the extremities. Treatment for syphilis was discontinued October 25.

Symmetrically distributed over the trunk and extremities, there is a hyperpigmented eruption, which is dry and topped by a thin scale. The lesions tend to be oval or irregular in contour. The vermilion border of the lower lip is depigmented. Leukoplakia is present on the tongue.

The Hinton and Wassermann reactions of the blood were positive. The urine and the blood sedimentation rate were normal. The routine examination of the blood showed hemoglobin content, 71 per cent, erythrocytes, 3,100,000, and leukocytes, 7,300, with 3 per cent eosinophils.

Treatment has consisted of the administration of calcium gluconate orally, a solution of liver extract intramuscularly, application of lotions and colloidal baths.

#### DISCUSSION

DR BERNARD APPEL, Lynn, Mass. I am inclined to believe that the history, the extent of the eruption, the residual pigmentation and the fact that the appearance of the dermatitis followed several doses of an arsenical produce a picture consistent with dermatitis medicamentosa due to arsenic.

DR WILLIAM R HILL, JR, Boston. The patient has vesicular lesions of the lichenoid type. I think that they are a postarsphenamine lichenoid eruption.

DR FRANCIS P MCCARTHY, Boston. Reference was made to the development of mucous patches in the mouth following use of arsphenamine. Whether or not

that was meant to be in the history, I do not know. The patient shows an advanced syphilitic glossitis, with atrophy and complete disappearance of the papillae of the tongue. A few islands of relatively normal papillae and a typical leukoplakia are present. These facts indicate a disease of long duration and are consistent with syphilis of long standing. The eruption in the mouth certainly could not have been a mucous patch occurring in a person with a disease of such duration. I think that it is part of the toxic effect of the arsenic.

DR AUSTIN W CHEEVER, Boston. I agree entirely with Dr McCarthy.

DR FRANCIS M THURMON, Boston. The oral lesions that the patient had were of an acute intermittent type, which occurred after the dermatitis had begun. They resembled mucous patches and lasted from seven to ten days. They were not the mucous patches seen in secondary syphilis. The patient has not responded to the prescribed therapy. The increase in pigmentation and number of lesions has continued. If there are any suggestions for therapy in this particular case, I should certainly be glad to hear them.

DR GEORGE E MORRIS, Boston. I suggest that the patient be given some typhoid vaccine along with an arsenical. I should like to see this woman again.

DR FRANCIS M THURMON, Boston. I should hesitate to administer a trivalent arsenical concurrently with induction of artificial fever, because I am not certain whether this eruption is due to syphilis or to an untoward effect from medication for syphilis.

#### A Case for Diagnosis (Parapsoriasis Lichenoides [Brocq]) Presented by DR WILLIAM P BOARDMAN, Boston

A C, a white American girl aged 15, presented a generalized and persistent erythematous eruption of two months' duration.

Generally distributed over the body are flat papular dark red to slightly brownish pigmented lesions. Similar lesions were sparsely present on the face. There is no scaling and no pruritus. Follicular lesions are seen on the extremities. Small lymph nodes of generalized distribution are palpable. The patient presents no oral lesions.

The Hinton reaction of the blood was negative on two occasions. The urine was normal. A routine examination of the blood showed hemoglobin content, 76 per cent, erythrocytes, 4,150,000, and leukocytes, 6,400, with a normal differential count.

#### DISCUSSION

DR BERNARD APPEL, Lynn, Mass. I agree with the diagnosis as presented. The unusual feature of this case is that the lesions are perhaps not quite as papular and do not show the crusting that one would expect in the more classic picture. The symptoms correspond to the generalized macular and papular nonitching eruption, which is rather slow to disappear, together with a negative serologic reaction, as is seen in the Brocq syndrome. So far as the eruption is concerned, the roseolate lesions are indistinguishable from secondary syphilis.

#### A Case for Diagnosis (Vitiligo, Scleroderma, Lichen Sclerosus et Atrophicus?) Presented by DR C GUY LANE, Boston

R S, a white youth, aged 19, presented lesions on the back, neck, extremities, tongue and buccal mucosa of five years' duration.

At the onset there were small red asymptomatic firm swellings, which appeared on the dorsum of the left hand. A local physician administered a bismuth preparation intramuscularly at weekly intervals for three months, with no improvement. A second physician administered liver extract, without improvement. The lesions slowly spread and appeared on the right hand. Loss of flexibility of the fingers was noticed. Two years ago Dr Arthur Greenwood administered roentgen rays over the sympathetic nerves in the thoracic region of the spine. Six months later biopsy, performed at the Burbank Hospital, Fitchburg, Mass., substantiated the previous diagnosis of lichen planus. Twelve months ago the patient noticed a tense firmness developing in the skin, which originally involved the hands and feet but slowly extended to include the legs, arms, face and neck. Articular motion became limited, atrophic changes of the skin occurred, ulcerations of the hands and feet developed, and loss of weight, malaise and easy fatigability were noted. Three months ago the entire body was involved, the feet were affected by lesions similar to those on the hands. Small reddish macular patches appeared on the tongue, which eventually became covered with dry scales. At the same time sharply margined pigmented and depigmented areas became evident over the body. Soreness of the tongue and especially of the lateral margins developed. There was alopecia of the scalp, and the hair after partial regrowth was white. Increasing loss of pedal and manual flexibility was accompanied by general malaise and weakness.

Examination revealed areas of pigmentation and depigmentation. The skin of the hands, forearms, feet and legs is tense, firm and smooth. Several ragged ulcerations are present on the dorsa of the feet and hands. Vesicles are present on the hands. The skin of the neck, axillae, cubital spaces and portions of the back is thick, tense, smooth, white and somewhat scaly. The prepuce is atrophic and ivory white, and phimosis is noted. The tongue is smooth. White atrophic areas are present on the buccal mucosa. There is decided limitation of motion of all distal extremities.

Laboratory studies revealed no abnormalities except a mild secondary anemia. Treatment has consisted of therapy with multiple vitamins, applications of chlorinated soda and the use of basic fuchsin.

DR C GUY LANE, Boston. This patient was seen by Dr Arthur Greenwood two years ago. I hoped that he would be here today. We both felt at that time that the patient definitely had lichen planus, but there were some unusual features about the case. I think that this case has been presented previously. It is difficult for me to correlate this present eruption with a previous lichen planus, and yet there are certain areas which suggest an atrophic lichen lesion. It seemed to me that this case belongs with those of scleroderma. I was interested to find in the "Corpus iconum morborum cutaneorum" edited by L. Nékam following the last International Dermatologic Congress, in Budapest, a photograph of an ankle looking like the patient's ankle in this case. The disease was classified as an ulcerated scleroderma. I do not know whether any of the lesions on the backs of the hands, which looked a great deal like small bullae in the beginning, have remained. If one looks closely at the right knee, one can see that vesicles have developed. There has been slight enlargement of the area during the period of observation, it has not been treated. It has been my belief that on the ankles and on the backs of the wrists the bullae have perhaps developed as a result of motion, and at these sites ulcerations have formed. I am not



optimistic with regard to therapy, but I shall be grateful for any suggestions

DR FRANCIS M THURMON, Boston I believe that a sympathectomy might be of benefit in this particular case

#### A Case for Diagnosis (Nevus Linearis?) Presented by DR AUSTIN W CHEEVER, Boston

M D, a Scotch boy aged 2 years, presented a lesion of two months' duration, extending from the right shoulder down the arm

The onset was marked by a small area over the anterior surface of the shoulder, which gradually extended toward the neck and down the arm

Examination reveals mottled slightly raised rough papules, reddish brown and 5 mm to 15 cm in diameter

#### DISCUSSION

DR JACOB H SWARTZ, Boston I suggest the diagnosis of lichen striatus, and I believe that the lesion should be left alone

DR AUSTIN W CHEEVER, Boston I accept the diagnosis I recall a similar case presented six months ago in which a large strip of the lesion had been removed surgically A disfiguring keloid developed and then faded, leaving a wide smooth scar Practically the whole of the lesion that was not removed surgically has disappeared, but a scar remains at the site of removal I wonder if this case is not of the same type

#### Lichen Nitidus Presented by DR AUSTIN W CHEEVER, Boston

A R, a 25 year old Greek man, presents an itching eruption involving the buttocks, thighs, genitocrural folds and extensor surface of the left forearm, of nine months' duration

The lesions were slow to develop, and there was considerable itching The lesion above the left knee has largely cleared, and the hair is regrowing The patches are slowly reddening and are made up of closely packed flat, dome-shaped papules, which are the color of normal skin

Biopsy confirmed the diagnosis of lichen nitidus

The eruption has improved under roentgen therapy and mildly stimulating ointments

#### DISCUSSION

DR C GUY LANE, Boston This case does not fit my concept of lichen nitidus The lesions seen in lichen nitidus are not apt to be crusted They occasionally occur on the arms They may be grouped flat papules which are asymptomatic I wonder whether this could be neurodermatitis or whether there has been some therapy which resulted in dermatitis

DR ELI WOOD C WEISE, Bridgeport, Conn I should like to substantiate the diagnosis of neurodermatitis I do not know exactly how to account for the lesions that resemble lichen nitidus Biopsy has been made at the Walter Reed Hospital Physicians there tend to favor the diagnosis of lichen nitidus or granuloma annulare The lesion which I palpated felt firm and almost keloid-like in structure

DR GEORGE SCHWARTZ, Boston The lesions on the buttocks and thighs suggest a contact dermatitis

DR LEONARD E ANDERSON, Springfield, Mass I should like to suggest that a test with congo red be done This might be a lichenoid papular type of circumscribed amyloidosis

DR JOHN G DOWNING Boston I do not agree with the diagnosis of lichen nitidus I have never

encountered a case of lichen nitidus in which the penis and the lower portion of the abdomen were not involved

DR AUSTIN W CHEEVER, Boston This is not my idea of lichen nitidus, but the patient has been seen by two dermatologists, who, I believe, saw the biopsy specimen and agreed that it showed lichen nitidus It seems strange to me that a contact dermatitis would produce such complete epilation The patient is extremely hairy The involved areas are almost bald A mild ointment of salicylic acid has been applied as well as a tar ointment and boric acid ointment As yet I have not had the opportunity of studying this case thoroughly

## LOS ANGELES DERMATOLOGICAL SOCIETY

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*April 11, 1944*

#### A Case for Diagnosis (Late Syphilis?) Presented by DR CHRIS HALLORAN

A F F, a Mexican man aged 55, has an eruption which began about one year ago, on the hands The first lesion was under his heavy signet ring on the fourth finger of the left hand At about the same time four furuncle-like lesions appeared on the back These were incised by a physician in Mexico City Soon after that, four other lesions, that were suggestive of leprosy, appeared on the legs The lesions on the back discharged a serous pus for three or four months and finally healed The lesions on the legs have healed except for one coin-sized ulcer There is an annular margined silver dollar-sized lesion on the back of the left wrist There are lesions on the bearded region that tend to be circinate and are impetiginous at times

The Wassermann reaction of the blood was negative The urine was normal Microscopic examination of the purulent discharge, on smear preparation and on culture, showed streptococci, *Streptococcus viridans* and staphylococci Nasal smears have not revealed Hansen's bacilli (*Mycobacterium leprae*)

#### DISCUSSION

DR H C L LINDSAY The lesions on the wrist look like ringworm

DR NELSON PAUL ANDERSON I think that all one can say is that the lesions belong in the granuloma group Biopsy should be done Apparently syphilis has been excluded I doubt that one can say much more before further investigative work has been done

DR H P JACOBSON The eruption in this case presents features strongly suggestive of psoriasiform syphilis The negative serologic reaction does not exclude that diagnosis The lesions on the face are fairly superficial, and slight atrophy and a lesion suggestive of lupus erythematosus are evident on the left side The diagnosis rests between psoriasiform syphilis and lupus erythematosus, and a therapeutic test should help to establish the definite diagnosis

DR PAUL FOSTER It strikes me that in this case there is the clinical picture of something with which I am not familiar In view of the fact that the patient has spent a number of years in Mexico, it seems to me to be advisable to investigate the possibility of pinta



DR M E OBERMAYER Dyschromic changes, though microscopically demonstrable during the early stages of pinta, become visible to the naked eye only much later

DR CHRIS HALLORAN One is impressed with the multiplicity of types of lesions. Some of them behave as furuncles. Those on the legs suggest erythema induratum. The lesions of the bearded region resemble impetigo at times. It may be tertiary syphilis with a negative Wassermann reaction. Pinta would cause a positive Wassermann reaction of the blood.

#### Lichen Sclerosus et Atrophicus Presented by DR MOLLEURUS COUPERUS

I S, a white woman aged 52, two years ago noticed small white spots, which appeared on both sides of the neck. There was some itching. Six months later similar spots appeared on the elbows, and since then similar spots have appeared on the shoulders, arms and legs. At no time were the lesions any other color but white, and none have disappeared.

The general appearance is that of a healthy woman approximately 50 years old, who is in no apparent discomfort. There are many lesions, pinhead to lentil sized, they are white to ivory, flat, firm and polygonal or round and papular. They are most numerous at the sides of the neck, on the shoulders and over the scapular region of the back. There are a few lesions on the flexor surfaces of the elbows and knees and on the arms. There are no oral lesions. Most of the lesions have a slightly raised margin. All are smooth except for the presence of follicular keratotic plugs in many of them. Others have a central depression. Some of the lesions are atrophic and slightly depressed. The lesions tend to be discrete, but over the scapular area there is a tendency toward confluence, though even there each lesion is distinguishable.

The Wassermann reaction of the blood was negative. Biopsy of one of the larger lesions showed a thinning of the epidermis, with the prickle cell layer thinned to 2 or 3 cells, and an increase in the thickness of the stratum corneum. The basal cell layer was considerably disorganized in architecture. The rete pegs were absent. In the upper half of the cutis in this area there was considerable homogenization of the connective tissue, with a reduction in nuclei and an absence of cellular infiltrate. In the lower half of the cutis there was a dilatation of lymph vessels and some irregular tissue, apparently not connected with any vascular structures. In this part of the cutis some fragmentation of connective tissue fibers and a moderate amount of lymphocytic cellular infiltration occurred. The Weigert stain showed an absence of elastic tissue in the upper part of the cutis and some clumping and a condensation of elastic tissue fibers around the tissue spaces in the middle and lower parts of the cutis.

#### Sarcoid Presented by DR SAMUEL AYERS JR

V S, a white woman aged 32, has had lesions scattered over the body for five years. The first lesion began five years ago on the back of the right hand, and it has persisted. Six months ago it was treated by electrodesiccation. During the past four months four other lesions have appeared. They produce no discomfort. On the back of the right hand, between the knuckles of the second and third fingers, is an approximately dime-sized ill defined erythematous somewhat atrophic area without infiltration. This is the oldest lesion, and has previously been treated by

electrodesiccation. A lesion is present on the outer aspects of each arm, consisting of ill defined approximately dime-sized, irregular and slightly infiltrated plaques. These have a lobulated appearance, a suggestion of yellowish color and small dilated capillaries. On the right buttock is a well defined erythematous lesion. On the forehead, just below the hair line, is an irregular half-dime-sized superficial dry lesion with a rough surface.

Biopsy of one of the lesions on the arm suggests a deep sarcoid. Located deep in the cutis are nests of cellular infiltrate composed of small round cells and pale-staining epithelioid cells.

#### DISCUSSION

DR ANKER JENSEN I saw this woman about five years ago. At that time she had a lesion on the back of her right hand. I suggested that a biopsy be done, but she failed to return.

DR SAMUEL AYERS When I first saw her the only two diagnoses I thought of were a peculiar xanthoma or a sarcoid of some type. Biopsy confirms the diagnosis of sarcoid.

#### A Case for Diagnosis (Blastomycosis, Sporotrichosis?) Presented by DR ANKER K JENSEN

I L is a Danish woman, aged 54 years. About four months ago she bruised the back of her left hand by striking it on the edge of a table. About two weeks later the back of her hand began to swell. Since then it has been treated with ointments and wet dressings locally. The swelling has been opened and drained surgically, with no improvement. The patient states that there are always numerous pinhead-sized pustules scattered over the area. At the elbow are two firm nodules. There is a dark red quarter-sized ulcer on the dorsum of the left hand. Its margins are sloping. Scattered over the surface of the ulcer are numerous pinhead-sized yellowish pustules.

The blood cells were normal. A tuberculin patch test elicited a negative reaction. The Wassermann reaction of the blood was negative on two occasions. The urine was normal.

#### DISCUSSION

DR M E OBERMAYER All that can be said without biopsy is that the lesion is a chronic infectious granuloma, possibly due to fungous infection.

DR SAMUEL AYERS There is a possibility of its being a primary tuberculous chancre. The lesion is of four months' duration, and a lymph node is palpable at the bend of the elbow.

DR H P JACOBSON Morphologically the presenting lesion shows nothing to suggest the diagnosis of blastomycosis. Nor, for that matter, is the clinical history in any way suggestive. Blastomycosis in this part of the country is extremely rare. I recall only 1 case in my entire experience in which there was a history of infection acquired locally. The presenting lesion consists of a central crust surrounded by an inflammatory zone with involvement of most of the underlying soft tissues but with no peripheral vesicopustules. This lesion is certainly inflammatory, but it is not blastomycosis.

DR PAUL FOSTER The patient had palpable lymph nodes all the way up her arm. The first one began at the elbow. I think that sporotrichosis should be considered as well as primary tuberculosis. She also had several roentgenograms taken of that hand, but

she was unable to state whether fluoroscopic examination of the hand had been made or not. The lesion looked somewhat like roentgen dermatitis, and I think that this possibility should be remembered in future observations.

DR H J TEMPLETON Could not the lesion be called a pseudo chancroidal pyoderma?

DR ANKER JENSEN The lesion has changed somewhat since the first time I saw the patient. At that time it was elevated about  $\frac{1}{4}$  inch (0.6 cm), with well margined sloping borders. When tension was applied to the lesion, small droplets of pus appeared throughout the area. It looked like a classic lesion of blastomycosis although I was doubtful of that diagnosis. Blood counts were within normal limits, the Wassermann reaction was repeatedly negative, and smears and cultures revealed no pathogens. No organisms were seen on microscopic examination of a potassium hydroxide preparation.

#### A Case for Diagnosis (Lichen Planus, Lupus Erythematosus?) Presented by DR W H GOECKERMAN and DR L F X WILHELM

T C P, a white married woman aged 55, began to have a burning eruption around the nails about a year ago. There has been almost no local sensation, such as itching. Her general physical condition is good. There is erythema with telangiectasia around the nails and erythematous patches on the hands. Some of these lesions are atrophic. There is some redness of the eyelids. The elbows have erythematous areas.

Bismarsen has been given intramuscularly for several weeks, without apparent improvement.

#### DISCUSSION

DR NELSON PAUL ANDERSON I feel that the eruption is lupus erythematosus. There is a disseminated type of lupus erythematosus which starts with a peculiar discoloration at the base of the nails and in which facial lesions later appear. If there is a low white blood cell count, it will substantiate such a diagnosis. I should hesitate to let the patient be exposed to much sunlight.

DR KENDAL FROST My diagnostic impression is that this is lichen planus of the finger tips and eyelids.

DR M E OBERMAYER I appreciate Dr Nelson Anderson's remarks on lupus erythematosus. The resemblance of the lesions to lupus erythematosus is close, yet there are several plaques on the dorsa of the fingers which on close inspection revealed the presence of confluent flat shiny papules. I believe that microscopic examination would prove the correctness of the diagnosis of lichen planus.

DR SAMUEL AYRES I agree with Dr Obermayer that the occurrence of those little flat papules, especially those running along the fingers and sides of the hand, are typical of lichen planus. It is rather strange that lichen planus which has persisted for as long as one and a half years has not affected the nail, because in the last month I have encountered 2 cases of lichen planus in which the nails were involved, with much resulting deformity. Biopsy should be done.

#### A Case for Diagnosis (Erythema Multiforme?) Presented by DR KENDAL FROST

M M, a white woman aged 36, has lesions on the forearms and one on the center of the back. The latter has been present for two years, but the lesions on the forearms appeared about five weeks ago. The lesion

on the right forearm began as a small papule, and the one on the left began in a scratch. Both developed gradually to their present size. There has been no pain and no itching. The patient had some lesions on the right arm and on the sides of the neck last year, but she believes that they were not similar to the present ones. They disappeared spontaneously. She says that she has not taken any drugs. Her general health is good.

There is a circinate lesion on each forearm. The margins of the lesions are bluish red, sharp, elevated and cordlike. In the center of the back is an oval bluish, lichenified, scaly lesion, about 5 cm in its longest diameter. A new spot, about 1 cm in diameter, developed four days ago over the inner end of the left clavicle. It corresponds to the two larger lesions on the forearms.

A specimen for biopsy was removed from the left forearm two weeks ago, and the following conditions were noted. The stratum corneum was uniform and narrow. The stratum granulosum was no more than one layer in thickness and was missing entirely in places. The prickle cell layer showed some degree of spongiosis in its upper portion. There was liquefaction necrosis in the basal layer. Polymorphonuclear leukocytes were scattered through the epidermal layers. The dermis was edematous, and its blood vessels were dilated. It also had a moderately dense infiltrate blending in with the basal cell layer. This infiltrate consisted of lymphocytes and polymorphonuclear leukocytes, and in the deeper portion of the dermis there were small numbers of epithelial cells.

#### DISCUSSION

DR CHRIS HALLORAN The lesion on the back has been present for a couple of years. I believe that that is a neurodermatitis. The acute lesions on the arm impress me as being a fixed drug eruption.

DR NELSON PAUL ANDERSON I do not believe that a fixed drug eruption can produce this picture, even when the person continues to take the drug. On the left forearm is the site from which the biopsy specimen was taken, by Dr Frost several days ago. Now this site is well inside the circumference of the lesion. Its borders are definitely firm and infiltrated. I cannot believe that a drug can produce the eruption presented by this patient.

DR H C L LINDSAY A granuloma due to bromides can produce a raised border somewhat like this.

DR M E OBERMAYER Dr Nelson Paul Anderson emphasized the mode of spreading of the lesions. Peripheral extension with recurrences in the center while the lesion is still extending and subsequent formation of concentric rings are features characteristic only of the erythema multiforme group with the cases of which this one should be classified. Whether the eruption in this patient is caused by a focal infection or by hypersensitivity to a drug cannot be determined at this time, but the clinical diagnosis is erythema multiforme.

DR H P JACOBSON Dr Anderson has brought out a vital point regarding the morphologic features of this eruption. The advancing, sharply margined borders of the elevated erythematous patches suggest an infectious or a toxic factor. The patches appear somewhat infiltrated. I should entirely discard the possibility of dermatitis factitia.

DR PAUL FOSTER I think that this case is one of fixed drug eruption, but what the drug was I cannot say. The patient stated that she had taken only

vitamin B I have never seen vitamin B alone produce such an extensive group of lesions. It should be noted that this patient also has a lichen chronicus simplex type of lesion in the central portion of her back. Probably this has nothing to do with the new acute lesions on her forearms.

DR SAMUEL AYRES The patient has been using a Vapex inhaler, in which there are a large number of drugs. If she had been using this for some time every day, it could account for a drug eruption which would spread and enlarge.

DR L F X WILHELM My first impression was that this is a dermatitis factitia, but now, after discussing the case with Dr Frost, I favor the diagnosis of multiform erythema.

DR KENDAL FROST I am grateful for the discussion. When I first saw these lesions I felt certain that they were a drug eruption, but I could get no history of her having taken drugs. Biopsy was performed. Examination of the slide did not reveal any changes that assisted in the diagnosis. I am certain that the eruption belongs to the multiform erythema group. The part which puzzled me was the rapid spread of the lesions.

NOTE—After an intravenous injection of calcium thiosulfate solution, the lesions stopped spreading and no new ones appeared within forty-eight hours. The case turned out definitely to be one of ordinary multiform erythema.

#### Oil Acne of an Unusual Type Presented by DR NELSON PAUL ANDERSON

M T, a white woman aged 43, is employed as a lathe operator, while she is working her hands and forearms become oily. She has an occasional pimple on the face. The present eruption began four months ago on the face and forearms. She first noticed that pores on her forearms were black, and then she began to have blackheads on the cheeks and forehead. She has worked with machine oils for the past ten months.

The forearms have numerous black follicular orifices. The sides of her face, especially in the malar regions, present a peculiar reticulated pigmented eruption. The pigmented part is macular.

#### DISCUSSION

DR HAL E FREEMAN I suggest that there may be more here than oil acne. There is also a melanosis, perhaps Riehl's type, on the face.

DR L F X WILHELM I have encountered 1 or 2 cases of the same type of eruption recently in women working in defense plants.

DR SAMUEL AYRES I think that this is an interesting case because of the distribution of the lesions. I have seen a few patients with oil acne, but I have never seen one with the eruption on the face. It is practically always on the arms and legs, where the oil has got on the skin. This patient has only a few lesions on the arms, yet she works with her sleeves up.

DR ANKER JENSEN This woman reminds me of a patient I had with oil acne. His skin was so covered with comedos that he had taken on a grayish slate color. As soon as his job was changed and he no longer contacted oil, his eruption cleared.

DR A FLETCHER HALL I have never seen anything like this eruption on the face that I should associate with oil. I agree with Dr Freeman that there is something else on the face. I am not inclined to associate it with oil acne.

DR NELSON PAUL ANDERSON I hope that you did not get the impression that I think that this eruption is an ordinary oil acne, because I do not. The only similarity is the oil folliculitis on the forearms. I do feel that the changes in both malar regions and the peculiar melanosis are due to oil plus some other factor, possibly sunlight.

#### A Case for Diagnosis (Epithelioma of Lip?) Presented by DR A FLETCHER HALL

C R L, a white man aged 40, is employed as a molder in an aircraft plant. Five years ago he had a lesion on the lip similar to the one there today. This was burnt off with an electric needle by a physician, who stated that the lesion was a "precancer." It was well until four months ago, when the skin "broke" and a pitted ulcer began. He states that the lesion seems to vary in size, with a definite cycle of five or six days. It is located just to the left of the middle of the lower lip. The vermilion border is affected by an abrupt umbilication, about 3 mm in diameter, at the bottom of which is a fine verrucous type of lesion. The lesion is palpable through the thickness of the lip as a moderately infiltrated tumor.

#### DISCUSSION

DR KENDAL FROST The diagnosis cannot be made without biopsy. I have seen a few lesions of this type which I am certain were rapidly developing warts with an epithelial proliferation that formed the annular smooth elevation surrounding the central depression in which the wart is situated.

DR H P JACOBSON The presenting lesion shows all the characteristics of epithelioma of the lip. The central ulceration is surrounded by a zone of deep solid infiltration, which is more suggestive of epithelioma. There is also an enlarged palpable submental node, which I believe represents metastasis.

DR H C L LINDSAY The lesion certainly looks and feels like an epithelioma. However, the man says that it varies in size from time to time and sometimes is much worse than others. Such a history would be inconsistent with a diagnosis of epithelioma.

DR A FLETCHER HALL I am not willing to make a diagnosis, as I indicated by my question mark. I was interested in Dr Jacobson's and Dr Frost's remarks, because the difference between their suggestions is so wide. If biopsy is to be performed in the manner suggested, it will really be a surgical procedure and certainly not a dermatologist's job. The whole question is whether there is justification for sending this man to have a wedge-shaped excision, which would have to be rather deep.

DR SAMUEL AYRES I do not see any particular indication for a wedge-shaped excision. This is a small lesion, no larger than a pea. It will granulate inward and leave little scarring. If there is a lymph node there, it should be excised, but as far as the main lesion is concerned, I think that the chances are 99 to 1 that it is an epithelioma. I think that it could be removed in a cylinder-shaped piece of tissue by means of a cutting current.

#### A Case for Diagnosis (Rosacea?) Presented by DR SAMUEL AYRES JR

E E, a white woman aged 29, about two years ago had her first attack of the present disease, which started with redness, pimples and pustules on the chin, cheeks and nose. The appearance of the lesions seemed

to be associated with a "stopped up" nose. After two months the eruption cleared. She had two more attacks, one about one and a half years ago and another one year ago. The latter was associated with a miscarriage. About six weeks ago the patient had an acute infection of the respiratory tract with a febrile reaction, and the present eruption appeared. There is burning and throbbing. She says that she has not taken iodides or bromides except one dose of elixir of three bromides N F two months ago. The lesions have spread onto the neck, chest, back and arms.

Her mother had similar lesions at intervals up to the age of 25. The patient had dengue in 1935. She is very nervous. The lesions are limited to the face and are thickly distributed over the medial portion of the left cheek, the lower portion of the nose and the chin. There is diffuse redness with several deep papulopustules.

*Demodex folliculorum* has been readily demonstrated by microscopic examination of selected scales from the face on three separate visits.

The patient is receiving fractional weekly doses of roentgen rays. Injections of autogenous vaccine are being given, and she has been instructed in the use of a sulfur-containing ointment (Danish ointment) locally.

#### DISCUSSION

DR M E OBERMAYER This case is interesting not only because the rosacea syndrome is pronounced in the extreme but because acneiform and pustular lesions, which, however, are not *acne vulgaris*, are present on the chest and back. I have occasionally observed spectacular results in cases of such pronounced rosacea from the administration of dilute hydrochloric acid or glutamic acid hydrochloride, the doses should be high and should gradually be increased up to the limit of tolerance.

DR SAMUEL AYRES I think that this case is extremely interesting from two points of view: the violence of the eruption and the recent dissemination. Until two weeks ago the eruption was localized on the face. In the last two weeks lesions have appeared on the shoulders, arms and chest, which have been papular. I have never seen rosacea behave this way although I made that diagnosis in the first place. I think that this eruption may be an unusual form of lupus erythematosus or some other toxic eruption.

#### Tinea Amiantacea Presented by DR NELSON PAUL ANDERSON

M A, a 46 year old white woman, has had an eruption of the scalp for the past fourteen months. It began behind the left ear and in the left groin. There is a scaly crusted eruption on the scalp, which gives the appearance of dry, grayish scales climbing up the hair shafts.

No fungi were demonstrated by direct microscopic examination.

#### DISCUSSION

DR H C L LINDSAY The lesion looks and smells like taurus, but typical scutula are not present.

DR M E OBERMAYER I agree with the diagnosis, yet it is only a descriptive label for a disease which cannot be classified because of lack of knowledge as to its cause.

#### A Case for Diagnosis (Cutaneous Atrophy) Presented by DR SAMUEL AYRES JR

L H, a white man aged 25 has lesions, of three years' duration, scattered over the body. He complains

of gradual loss of hair from the scalp and body during the past four years. There are no subjective symptoms.

Lesions are scattered over the trunk and the arms, which consist of about six irregular patches varying from half-dollar size to hand size. Some lesions are almost imperceptible, but older ones are pronounced. The older lesions are of a pale violaceous color, with a faint suggestion of atrophy, and are evident on the anterior aspect of the right arm and near the center of the chest. On the posterior aspect of the left arm, beginning on the back of the shoulder and extending down on to the arm, is an irregular lesion with a definite scarlike appearance in the upper portion. Across the lower part of the back is an area, twice the size of a hand, extending onto the right side of the trunk. This shows a wide peripheral zone of a violaceous color and a large central area of whitish atrophy. Within the white atrophic area the hair follicles appear to be preserved and stand out in somewhat darker contrast to the whitish background. No infiltration is observed in any of the areas. The scalp hair appears to be not abnormal, and its loss appears to be nothing more than an average type of premature but natural alopecia. The pubic hair appears normal, but the patient says that it has become thinner than formerly.

The Kahn and Kline reactions of the blood were negative.

#### DISCUSSION

DR KENDAL FROST I think that this is a case of morphea.

DR L F X WILHELM I agree with Dr Frost.

DR MOILERUS COUPERUS I do not know whether it should be classified with cases of the pseudosclerodermatous type of atrophy or not. I was of the impression at first that this was a case of scleroderma, but on feeling the lesions, I do not know of any better designation than cutaneous atrophy.

DR CLEMENT COUNTER I agree with the diagnosis of morphea. Particularly the lesion on the back at the level of the beltline suggests that diagnosis. It has a violaceous border, and the central portion is thicker than the unaffected skin nearby, even though that increase in thickness is not so great as is common in cases of more typical localized scleroderma.

DR SAMUEL AYRES JR I think that these differentiations are largely a matter of definition. I have always considered morphea to be a localized scleroderma with thickening of the skin. These lesions have not, as far as I can tell, any induration in them. There seems to be simple atrophy, with no induration. Perhaps the definition of morphea may be at fault. As one looks at the eruption, I think that one would not make any other diagnosis than morphea, but when palpated, it shows no induration. It is probably closely related to morphea.

#### A Case for Diagnosis (Pellagra, Pityriasis Rubra Pilaris?) Presented by DR ANKER K JENSEN

C A B is a white girl aged 9 years. Her present illness began about two years ago. The eruption began around the mouth, and then it occurred on the hands. It has remained limited to these exposed surfaces. The patient has received six months' treatment with vitamin A. During this time the dosage was 100,000 units daily. She also took 1 gram (0.06 Gm) of thyroid daily.

The skin of the involved areas is rough. In places it feels as if there were small firm spicules in the follicles. Other areas are colored a deep brown. The

rough areas that are not deeply pigmented are covered with dry desquamation

Biopsy showed most of the changes as occurring in the epidermis. There was hyperkeratosis, especially evident at follicular orifices. Irregular dyskeratosis was present in the epidermis around follicular orifices. There were lacunas in that part of the rete mucosum which showed the greatest irregularity of keratinization. The corium had a sparse cellular infiltration, most of which was perivascular.

#### DISCUSSION

DR CHRIS HALLORAN I could not make up my mind about the diagnosis in this case. It may be Darier's disease (keratosis follicularis), but the lesions on the fingers do not impress me as such. I do not believe it is pityriasis rubra pilaris.

DR NELSON PAUL ANDERSON I think that it is Darier's disease.

DR KENDAL FROST I believe that it is pityriasis rubra pilaris.

DR M E OBERMAYER I agree with Dr Frost. The groups of small keratotic papules on the dorsal surfaces of the phalanges are suggestive.

DR SAMUEL AYRES I think that it is Darier's disease.

DR L F X WILHELM I think that it is pityriasis rubra pilaris.

DR W H GOECKERMAN I consider it to be a case of typical Darier's disease.

DR ANKER JENSEN This patient's eruption seems to be more prevalent on the exposed surface of the body. This fact made me wonder whether possibly the sun had anything to do with the cause or whether vitamin A deficiency is more evident where the skin is exposed to the sunshine.

## INTENSIVE ARSENOTHERAPY OF EARLY SYPHILIS

LOREN W SHAFFER, M D

DETROIT

Many modifications of intensive arsenotherapy have been introduced since the original five-day slow intravenous drip method was announced by Hyman, Chargin and Leifer.<sup>1</sup> Further observations and reports on intensive methods have shown certain hazards, weaknesses, advantages and trends with such therapy. It is generally accepted that these methods compare favorably in efficiency with the older standard treatment of the eighteen month type. Excellent summaries on the present status of intensive arsenotherapy for early syphilis by Cole, Heisel and Stroud<sup>2</sup> and McDermott<sup>3</sup> are available.

The recent introduction of penicillin into the treatment of syphilis has confused still further the present chaotic state as to what is the most effective treatment of early syphilis today. This has occurred at a time when some semblance of fact is developing out of what must still be considered as experimental methods of intensive arsenotherapy. One can only await further developments with great interest. Possible combinations of arsenic, bismuth and penicillin may be the final solution to a safer and more effective cure for all types of syphilis. Physicians, therefore, in their enthusiasm for penicillin should not lose sight of the recent advances made in the rapid treatment of early syphilis by arsenotherapy.

Read at the Sixty-Fifth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 20, 1944

1 Hyman, H T, Chargin, L, and Leifer, W. Massive Dose Arsenotherapy of Syphilis by the Intravenous Drip Method. Five Year Observations, *Am J M Sc* **197**:480-485 (April) 1939. Hyman, H T, Chargin, L, Rice, J L, and Leifer, W. Massive Dose Chemotherapy of Early Syphilis by the Intravenous Drip Method, *J A M A* **113**:1208-1215 (Sept 23) 1939. Leifer, W, Chargin, L, and Hyman, H T. Massive Dose Arsenotherapy of Early Syphilis by Intravenous Drip Method. Recapitulation of Data (1933 to 1941), *ibid* **117**:1154-1160 (Oct 4) 1941.

2 Cole, H N, Heisel, E B, and Stroud, G. Intensive Methods of Treating Syphilis, *J A M A* **123**:253-258 (Oct 2) 1943.

3 McDermott, W. Recent Advances in the Treatment of Syphilis, *M Clin North America* **28**:293-307 (March) 1944.

The various types of rapid treatment are exemplified in the slow drip method (Hyman, Chargin and Leifer), syringe technic (Schoch,<sup>4</sup> Thomas<sup>5</sup> and Trow<sup>6</sup>), multiple injections (Eagle and Hogan<sup>7</sup>), and fever therapy plus arsenicals (Thomas,<sup>5</sup> Simpson and Kendall<sup>8</sup>).

According to the evaluation of massive arsenotherapy for syphilis by the United States Public Health Service,<sup>9</sup> presented at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 12 to 17, 1944, the statistics presented in table 1, obtained from 4,351 cases of patients treated in twenty-two cooperating clinics by the technics outlined, apply.

The best results were secured by the original slow drip administration of neoarsphenamine, but the drug is too toxic for its use to be continued, the next best were obtained by multiple injection of oxophenarsine hydrochloride (ma-

4 Schoch, A, and Alexander, L J. Short Term Intensive Arsenotherapy of Early Syphilis, *Am J Syph, Gonorr & Ven Dis* **25**:607-609 (Sept) 1941. Schoch, A G, and Alexander, L J. Intensive Arsenotherapy of Early Syphilis, *Arch Dermat & Syph* **46**:128-129 (July) 1942.

5 Thomas, E W, and Wexler, G. Rapid Treatment of Early Syphilis. Report of Two Hundred and Eighty Treatment Courses Alone and Five Hundred and Forty-Nine Treatment Courses with Mapharsen Combined with Fever, *Arch Dermat & Syph* **47**:553-568 (April) 1943. Hammond, R J; MacPhail, J A, and Thomas, E W. Results of Follow-Up of Patients Treated for Early Syphilis by Rapid Methods at Bellevue Hospital, *Ven Dis Inform* **24**:215-217 (Aug) 1943.

6 Trow, E J. Personal communication to the author.

7 Eagle, H, and Hogan, R B. An Experimental Evaluation of Intensive Methods for the Treatment of Early Syphilis. III. Clinical Implications, *Ven Dis Inform* **24**:159-170 (June) 1943.

8 Simpson, W M, Kendall, H W., and Rose, D L. Developments in the Treatment of Syphilis with Artificial Fever Therapy Combined with Chemotherapy During the Past Decade, *Brit J Ven Dis* **17**:1-66 (Jan-April) 1941.

9 Massive Arsenotherapy for Syphilis. United States Public Health Service Evaluation, Cooperating Clinics of New York and Midwestern Groups, *J A M A* **126**:554-557 (Oct 28) 1944.

pharsen) plus typhoid vaccine There is little difference in results obtained with oxophenarsine hydrochloride by slow or rapid drip or by multiple injection The poorest results were reported from multiple injections of old arsphenamine

The rapid drip method mentioned was that employed by the Social Hygiene Clinic of the Detroit Department of Health A total of 417 patients were treated by this method from December 1939 to July 1942 One death occurred in the series from toxic encephalitis, and in another case toxic encephalitis developed but the patient recovered Because of these reactions, results that were not too satisfactory and loss of our resident physician, this five day method was discontinued in favor of ambulatory intensive treatment

It was also concluded from this evaluation that patients over 25 years of age responded better than patients under 25, male patients better than female and white patients better than nonwhite

TABLE 1—Results in 4,351 Cases of Syphilis

| Method of Treatment   | Percentage of Satisfactory Results |                    |
|---|------------------------------------|--------------------|
|   | Primary Syphilis                   | Secondary Syphilis |
| Slow drip neoarsphenamine   | 89.5                               | 85.7               |
| Slow drip oxophenarsine hydrochloride                               | 85.7                               | 71.8               |
| Rapid drip oxophenarsine hydrochloride                              | 85.4                               | 64.5               |
| Multiple injection oxophenarsine hydrochloride                      | 85.4                               | 72.3               |
| Multiple injection oxophenarsine hydrochloride plus typhoid vaccine | 88.5                               | 70.2               |
| Multiple injection old arsphenamine                                 | 78.6                               | 56.7               |

The five day slow drip method is satisfactory as far as results are concerned A morbidity rate of 1 per cent and a mortality rate of 0.3 per cent from toxic encephalitis even in the best clinics indicate that the method is too toxic in its present form Modifications, such as that now being used by Wile,<sup>10</sup> consisting of administration of a total dose of 1,080 mg of oxophenarsine hydrochloride given over a period of eight days plus larger doses of bismuth, may minimize this hazard There is urgent need for a rapid method that can be completed during a reasonable period of hospitalization because of failure to hold average clinic patients to even an eight week course of ambulatory treatment, as well as for those patients requiring quarantine Modifications of the Wile type may prove a satisfactory substitute Likewise, multiple injections of the Schoch-Thomas type completed in a six to ten day period have carried similar morbidity and mortality rates The recent report from the Chicago

Intensive Treatment Center<sup>11</sup> on patients treated with combinations of fever therapy plus arsenoxide is promising as well as those reported earlier by Thomas<sup>5</sup> However, if such a widespread disease as syphilis is to be controlled, simplified methods will be necessary

Ambulatory intensive treatment of the Eagle type offers great promise for general use because of its increased safety, simplicity and equally effective results Its chief weakness lies in the fact that so few patients of the types commonly attending the larger free clinics can be expected to carry it through on schedule

#### AMBULATORY INTENSIVE TREATMENT

Eagle and Hogan,<sup>12</sup> on the basis of extensive and painstaking experiments on the treatment of syphilis in rabbits, found that within a time limit of ten seconds to six weeks the total amount of oxophenarsine hydrochloride necessary to cure varied but little There was surprisingly little difference from a standpoint of therapeutic efficiency for a given total dose, whether it was administered over a period of a few hours, days or weeks or whether it was given by multiple injections or by continuous drip They called attention to the published data on infectious syphilis in human beings, that the same observations seem to hold true, i. e., that it takes somewhere around 1,200 mg of oxophenarsine hydrochloride to effect apparent cure whether the dose is given by five day intravenous drip or by multiple injections over a period of a few weeks

They found, however, that the margin of safety in terms of toxicity to animals was definitely increased in the longer systems and decreased in the shorter ones The margin of safety between the toxic and the therapeutic dose (chemotherapeutic index) may be increased continuously by prolonging the duration of treatment In other words, the total curative dose of oxophenarsine hydrochloride varies only slightly with the frequency and total duration of treatment, while the total tolerated dose varies directly with the time period over which the arsenical is administered They were able to predict rather accurately, when using a constant total curative

11 Bundesen, H. N., Bauer, T. J., Kendell, H. W., and others. Intensive Treatment of Gonorrhea and Syphilis. Organization, Objectives, Activities and Accomplishments of the Chicago Intensive Treatment Center, Preliminary Report, J. A. M. A. **123**: 816-820 (Nov. 27) 1943

12 Eagle, H., and Hogan, R. B. An Experimental Evaluation of Intensive Methods of Treatment of Early Syphilis. I. Toxicity and Excretion, Ven. Dis. Inform. **24**: 33-44 (Feb.) 1943, II. Therapeutic Efficiency and Margin of Safety, *ibid.* **24**: 69-79 (March) 1943

10 Wile, U. J. Personal communication to the author



dose for rabbits, the incidence of serious toxicity with a system of any given duration. They stated the belief, and, in general, experience indicates, that approximately the same ratios apply to human beings. Eagle and Hogan do not feel that schedules of five to ten days provide reasonable freedom from serious toxic reactions and deaths. On a basis of their results in rabbits, they predicted that injections of 60 mg of oxophenarsine hydrochloride (1 mg per kilogram of body weight) repeated three times weekly should be effective for human patients. Accordingly, in October 1941, they set up a large scale clinical study of triweekly injections over total periods ranging from four to twelve weeks, some of which were supplemented with bismuth. This study began with twelve cooperating clinics and has increased to some eighty clinics at present.

A report was given before the Section of Dermatology and Syphilology of the American Medical Association at the 1944 meeting in Chicago by Dr. Harry Eagle.<sup>13</sup> Preliminary information on the 4,800 patients treated with triweekly injections of oxophenarsine hydrochloride which Dr. Eagle kindly forwarded to me is interesting and instructive.

#### TOXICITY

Minor reactions (vomiting, headache, diarrhea or subjective complaints) which did not contraindicate continued treatment were observed in 16 per cent of the patients.

A characteristic syndrome developed in the second to fourth week in approximately 2 per cent of the patients. The symptoms included fever, toxic rash, vomiting, headache, conjunctivitis and facial edema observed in varying combinations. In approximately half of these cases it was necessary to discontinue treatment. There were 40 serious reactions occurring in 21 cases of jaundice, 7 of dermatitis, 5 of blood dyscrasias, 3 of nephritis, 2 of peripheral neuritis and 2 of toxic encephalopathy—a total of 0.8 per cent serious reactions. Four of these were fatal (2 cases of nephritis, 1 of toxic encephalopathy and 1 of jaundice). The mortality of 1/1,200 is remarkably close to that anticipated when the study began, but should be qualified in two respects.

There is reason to believe that at least 2 and perhaps 3 of these deaths were preventable in that in spite of definite premonitory symptoms treatment was continued at the same dosage level. The mortality of the triweekly schedule may therefore be 1/2,000 or less, rather than 1/1,200. In the second place, from the standpoint of military medicine, it is of interest that all toxic reactions were more common in women than in men, more common in Negroes than in white persons and more common in patients under 18 years of age.

13 Eagle, H. The Treatment of Early and Latent Syphilis in Nine to Twelve Weeks with Triweekly Injections of Mapharsen. A Preliminary Analysis of the Results of the First 4,823 Cases, J A M A 126 538-544 (Oct 28) 1944.

Thus all 4 fatalities were observed in Negro women 3 of them under 18. In men over 18, treatment had to be discontinued because of toxic reactions in less than 1 per cent, serious reactions occurred in only 0.5 per cent, and there were no deaths in 2,583 patients treated.

#### END RESULTS

The end results of the various treatment schedules have been gratifying if unexpected. The simultaneous administration of bismuth has had a surprising effect on the incidence of therapeutic failure and cure. In patients with primary and secondary syphilis who did not receive bismuth, the cumulative percentage of failures was 30 per cent, and the total dosage of oxophenarsine hydrochloride had relatively little effect. On the other hand, in those patients who received simultaneous injections of bismuth, there was a striking correlation between the end results and the amount of treatment. In the patients that received less than seven weeks of treatment, failures amounted to 25 per cent, in patients that received seven or more weeks of treatment, failures were only 8 to 9 per cent, and 89 per cent of the patients were "cured." In the latter group, approximately one third of the therapeutic failures took the form of serologic relapse or seroresistance, and in only 1 in 300 patients did syphilis of the central nervous system develop.

The final results were not demonstrably affected by race, sex, age or initial reagin titer. Although there was no striking difference between the end results in

TABLE 2—Ambulatory Intensive Plan

|  |  |
|--|--|
| 1 Oxophenarsine hydrochloride (0.05 to 0.07 Gm.) | Three times weekly for twenty doses (six and two thirds weeks) |
| 2 Bismuth subsalicylate (0.2 Gm.)                | Twice weekly for eight doses (four weeks)                      |
| 3 Oxophenarsine hydrochloride                    | Twice weekly for ten doses (five weeks)                        |

seronegative and seropositive primary or secondary syphilis, the most favorable results were obtained in the seropositive primary stage. The optimum schedule for the treatment of syphilis by triweekly injections of oxophenarsine hydrochloride consists of at least eight and preferably ten weeks of treatment, each dose of the drug to consist of approximately 1 mg per kilogram of weight (maximum of 80 and minimum of 40 mg per injection). There should be concomitant weekly intramuscular injections of bismuth (0.2 Gm of bismuth subsalicylate). On such a schedule one may anticipate approximately 90 per cent clinical and serologic "cures."

#### PERSONAL EXPERIENCE WITH AMBULATORY INTENSIVE TREATMENT

In December 1941, an ambulatory intensive method of treatment was started at the Social Hygiene Clinic of the Detroit Department of Health. The plan of treatment called for three injections of oxophenarsine hydrochloride given weekly for a total of twenty injections (six and two-thirds weeks). The recommended dose varied from 0.05 to 0.07 Gm, depending on weight. This course of twenty injections was followed by eight injections of bismuth salicylate.

0.2 Gm given twice weekly for four weeks. This course, in turn, was immediately followed by ten more arsenical treatments, given twice weekly for five weeks. The entire course called for a total of thirty injections of oxophenarsine hydrochloride and eight of bismuth subsalicylate given in a period of fifteen and two-thirds weeks.

A total of 210 patients with early syphilis were assigned to this method of treatment during the year 1942. Only 63 of the 210 patients completed the treatment with satisfactory regularity and remained under observation for six months or more. This problem of case holding will receive further discussion later.

An analysis of the 63 cases in which this treatment schedule and the six month observation period were completed may be summarized as follows:

|   |          |
|---|----------|
| Classification                            |          |
| Early primary                             | 28       |
| Seronegative                              | 10       |
| Seropositive                              | 18       |
| Secondary                                 | 30       |
| Recurrent secondary                       | 3        |
| Early latent                              | 2        |
| Completed treatment                       |          |
| With satisfactory regularity (16 weeks)   | 31       |
| Fairly satisfactory regularity (18 weeks) | 32       |
| End result                                |          |
| Negative clinically and serologically     | 56 (89%) |
| Seroresistant                             | 5 (8%)   |
| Clinical relapse                          | 2 (3%)   |
| Serologic relapse                         | 0        |

These figures correspond closely to those reported by Eagle.

#### REACTIONS

It was necessary to discontinue treatment for 7 patients because of reactions (4 gastrointestinal reactions, 1 urticaria, 1 dermatitis and 1 conjunctivitis, facial edema and fever of the type described by Eagle). In addition, 1 patient had jaundice, supposedly of the acute catarrhal type, and promptly recovered, and in 1 an acute nephritis developed, requiring three months' hospitalization before recovery. Both reactions occurred approximately one month after treatment was completed. The nephritis followed an alcoholic bout of one week's duration, and the alcohol may have been an etiologic factor.

Experience gained through one year's trial with this sixteen week intensive plan indicated that treatment of the majority of our clinic patients was not carried through to completion with satisfactory regularity, in spite of an aggressive program in case holding. Our end results were satisfactory and reactions were minimal. The plan could probably be recommended for private practice and for clinics having

a better case-holding record. It is a compromise between the twenty-six week Army plan<sup>14</sup> and the eight to ten week Eagle plan. I should now be inclined to increase the bismuth by giving one injection at weekly intervals during the last two weeks of the first course of arsenoxide and during the first two weeks of the second course.

#### EXPERIENCE WITH EAGLE PLAN OF EIGHT WEEK INTENSIVE THERAPY

To try a shorter schedule, we began the use of the eight week Eagle plan of intensive therapy in January 1943. A total of 352 patients were given three injections of oxophenarsine hydrochloride and one injection of bismuth subsalicylate a week for eight weeks between Jan 1 and July 1, 1943. A total of 194 of these patients did not complete the treatment, for reasons to be enumerated. Likewise, 49 patients who completed the treatment in a satisfactory manner either were lost or transferred before they had been observed for six months. The end results for the 109 remaining patients, who have been followed for six to seventeen months, are summarized in table 3.

If one considers only the cases of primary and secondary syphilis, the following figures apply to the group as a whole:

|                      |            |
|----------------------|------------|
| Total cases          | 68         |
| Good results         | 51 (75%)   |
| Questionable results | 10 (14.7%) |
| Failures             | 7 (10.3%)  |

A few words of explanation of the classifications in table 3 are indicated. "Good" means that the serologic reactions became negative and remained so throughout the period of observation and that the patient was clinically free from evidence of the disease. In general, experience in this clinic has confirmed the observation of other clinics, i. e., the rate of reversal has paralleled the quantitative titer present at the time treatment was begun. Examination of spinal fluids has been carried out for only about 50 per cent of these patients, since it was found that if this examination was insisted on patients discontinued their treatment or disappeared from observation. Incidentally, I was surprised to find so few positive spinal fluids (approximately 4 per cent) in these patients with early syphilis even when tested before or at the start of treatment. It is probable that a revision should be made in the textbooks concerning the incidence of positive spinal fluids in early syphilis.

14 Diagnosis and Treatment of the Venereal Diseases, Circular Letter 74, Army M. Bull., October 1942, no 64, pp 188-208.

"Questionable" results include those for patients whose standard Kahn reaction is negative but the presumptive Kahn reaction is still positive and a second group whose standard Kahn reaction ranges from a doubtful positive to 3 plus positive on a quantitative basis. It is expected that the great majority of these patients will progress to complete seronegativity. However, serologic and clinical relapses have occurred in a small number of such patients and the ultimate outcome must be considered questionable.

All patients with a quantitative Kahn titer of 4 or more units at the time of their last observation are classed as seroresistant and included in the "failure" group. It is probable that many of them will progress to seronegativity and that results for them need not be classed necessarily as failure.

our experience with various types of intensive therapy and well over a thousand patients treated, we have found that the prognosis depends on the duration of the disease. No failures have occurred with any type of intensive therapy used for any patient with seronegative primary syphilis treated in our clinic. This observation is not in accord with results reported from other clinics. No patient is placed in this group if he has any degree of seropositivity, whether at the start, during or immediately after completion of treatment. The total number of patients with seronegative primary syphilis treated, including our five day group, is sufficiently large (63) to be statistically significant. True seronegative primary syphilis should offer nearly 100 per cent chance of cure. The next most promising group is patients with seropositive primary syphilis, followed by those with secondary syphilis and

TABLE 3—Eight Week Eagle Plan (Detroit Experience)

| Classification          | Results    |              |                 |                |             |                     |
|-------------------------|------------|--------------|-----------------|----------------|-------------|---------------------|
|                         | Good       | Questionable |                 | Failure        |             |                     |
|                         | Negative   | K—P+         | K ± to<br>K +++ | Seroresistance | Serorelapse | Clinical<br>Relapse |
| Seronegative<br>Primary | 6 (100%)   |              |                 |                |             |                     |
| Seropositive<br>Primary | 23 (85.2%) | 2 (7.4%)     | 1 (3.7%)        | 1 (3.7%)       |             |                     |
|                         |            |              | 11.1%           |                |             |                     |
| Secondary               | 22 (62.8%) | 4 (11.4%)    | 3 (8.6%)        | 3 (8.6%)       | 0           | 3 (8.6%)            |
|                         |            |              | 20%             |                | 17.2%       |                     |
| Recurrent secondary     | 0          | 4 (57.1%)    | 1 (14.3%)       | 2 (28.6%)      |             |                     |
|                         |            |              | 71.4%           |                |             |                     |
| Early latent            | 2 (5.9%)   | 7 (20.6%)    | 6 (17.6%)       | 16 (47%)       | 1 (3%)      | 2 (5.9%)            |
|                         |            |              | 38.2%           |                | 55.9%       |                     |

Serologic relapse is at times difficult to define. Fluctuations in quantitative titer, such as "bounces" from 4 to 20 units or 20 to 40 units and prompt return to progressively lower readings, are of fairly frequent occurrence. They may represent simply the personal equation of the technician reading the test or insignificant fluctuations from day to day in patients' reagin titer. When serologic relapse occurs, it is of significant amount quantitatively and remains so. It is essential for the adequate follow-up of intensive therapy that quantitative tests be available.

Clinical relapse usually manifests itself in dark field-positive mucocutaneous lesions or relapse in the spinal fluid (neurorecurrence). It is nearly always preceded by serologic relapse.

The experience of my colleagues and me indicates that it is desirable in appraising results to classify the types of early syphilis present in patients receiving intensive therapy. Throughout

then those with recurrent secondary and with early latent syphilis, in order. Similar charts for other types of intensive therapy given in this clinic show this same trend. Likewise, our experience has not confirmed the statement made from other sources that results on retreatment of patients with clinical or serologic failure can be expected to be satisfactory. In our experience such patients generally have the resistant or relapsing type of disease, are apt to fail with retreatment and are candidates for further intensification if rapid methods are used.

It is questionable, on the basis of our experience, whether persons with early latent syphilis are suitable for intensive methods of treatment. At least during the period of our observation the serologic results have been disappointing. It is admitted that the period of observation has not been of sufficient length to permit adequate appraisal of our results. Furthermore, seronegativity may not be a satisfactory aim with this

group The question of persistent symptomatic arrest can be answered only by lifelong observation Many patients without a definite history of infection are classified in this group on the basis of their age, when they may actually have late latent or congenital syphilis without stigmas

*Reactions* Reactions in this group of patients have paralleled closely those reported by Eagle in his 4,800 patients Treatment was discontinued for 8 patients (2 for gastrointestinal and 2 for Eagle type reactions [conjunctivitis, edema, etc], 1 for dermatitis, 1 for urticaria, 1 for jaundice and 1 for nephritis) No fatal reactions occurred to our knowledge

The results for patients with secondary, recurrent secondary and early latent syphilis were not considered entirely satisfactory In July 1943, it was decided to prolong treatment of such patients according to the following schedule

Seronegative primary syphilis—eight weeks  
(twenty-four injections of oxophenarsine hydrochloride and eight of bismuth subsalicylate)

Seropositive primary syphilis—ten weeks  
(thirty injections of oxophenarsine hydrochloride and ten of bismuth subsalicylate)

Secondary, recurrent secondary and early latent syphilis—twelve weeks  
(thirty-six injections of oxophenarsine hydrochloride and twelve of bismuth subsalicylate)

*Observations with These Schedules*—There has not been sufficient length of observation on these patients (maximum of eight months after completion of treatment) to report the end results with any degree of accuracy Approximately 400 patients have been assigned to these schedules An even larger proportion of the patients belong in the group classified as having early latent syphilis Our ability, or rather lack of ability, to hold these patients to regular treatment and completion of their course has been slightly poorer than with the eight week schedule

Reactions have paralleled closely those previously reported One patient died from aplastic anemia The relationship to arsenical treatment in this case is rather questionable

The patient, a Negro woman aged 19, received five injections of oxophenarsine hydrochloride in our quarantine hospital She also had gonorrhea and received 60 grains (4 Gm) of sulfathiazole daily for five days She had rather severe gastrointestinal reactions and moderate fever after each treatment Pus, albumin and casts appeared in her urine, and a mild jaundice developed two days after her last treatment She was transferred to the city of Detroit Receiving Hospital at once A diagnosis of pyelonephritis and jaundice was made She was given 60 grains of sulfamerazine daily for seven days for the pyelonephritis The nephritis subsided, but the jaundice became more severe

Two weeks after her admission moderate cutaneous purpura and a blood picture of hemorrhagic purpura developed This became progressively worse, and she died one week later, in spite of blood transfusions, BAL (a preparation of secret formula for neutralizing the toxic action of arsenic, being investigated through the National Research Council) and supportive measures Autopsy was refused

The sulfonamide compounds may have been the most important etiologic factor in the case The question as to whether sulfonamide drugs should be administered to a patient who is receiving intensive arsenical therapy should be answered, since both gonorrhea and early syphilis are frequently present Fortunately, penicillin may prove to make the answer unnecessary

Accurate statistics are not available on the results of the twelve week schedule for secondary and early latent syphilis Definite impressions, however, have been gained Results have been satisfactory with the eight week schedule for seropositive primary syphilis The ten week schedule will probably not show any worth while improvement It has been disappointing that the same impression applies to the twelve week schedule There is little evidence to suggest that any material improvement in end results will follow the increase from twenty-four injections of oxophenarsine hydrochloride and eight of bismuth to thirty-six of oxophenarsine hydrochloride and twelve of bismuth in cases of secondary, recurrent and early latent syphilis Fortunately, there is hope that greater efficiency can be gained by increasing the amount of bismuth given during the eight week schedule Combinations with penicillin may supply the needed extra effect

#### CASE HOLDING

This problem of case holding is of such great importance in the management of syphilis in clinic patients that it warrants special discussion No one without experience in a large city clinic dealing almost entirely with Negro patients can appreciate this problem In the Detroit Health Department Clinic a staff of five male follow-up workers is employed for this purpose Follow-up of family cases is made by the nurses from the Health Centers Personal conferences are repeatedly conducted with our patients to explain the nature and seriousness of their disease and the need of continuous treatment Only a relatively small proportion of the patients are actually lost The disposition of the patients originally assigned to the sixteen week schedule previously discussed is typical of what happens with these patients In that group of 210 patients only 63 completed the treatment in a satisfactory man-

ner The disposition of the 147 patients that failed to do so was as follows

|  |            |
|--|------------|
| Transferred to private physicians before treatment was completed | 33 (22 4%) |
| Lost   | 27 (18 4%) |
| Transferred to weekly treatment schedule because of irregularity | 22 (15 %)  |
| Treatment too irregular to classify                              | 19 (12 9%) |
| Moved from city and transferred to another treatment agency      | 17 (11 6%) |
| Quarantined through probate court after treatment had lapsed     | 15 (10 2%) |
| Accepted into military service before treatment was completed    | 8 ( 5 4%)  |
| Discontinued treatment because of reactions                      | 6 ( 4 1%)  |

As shown by these figures, only about 30 per cent of patients in our clinic can be expected to carry to completion an ambulatory system of treatment in a satisfactory manner. It is at least consoling that even those patients that discontinued the schedule received more treatment than they would have in the same length of time with standard treatment. The 33 patients referred to private physicians reflect improved local economic conditions and the policy of referring patients who are financially able to pay to private physicians for care.

These figures offer conclusive evidence of the need for shorter courses of treatment under hospital management if schedules are to be carried out as planned. Such patients would at least receive the treatment. If it was of maximum efficiency the fact that they would soon disappear from follow-up would be of minor consequence except from a statistical standpoint. The expense of hospitalization would be less than that for prolonged clinic care and support of follow-up workers. The hazard of such treatment is certainly less than the hazard of the disease inadequately treated. The hazard to public health presented by these inadequately treated patients, with their increased potentiality to relapse, has not been appreciated. Smaller total doses of oxophenarsine hydrochloride (750 to 1,000 mg) over an eight to ten day period plus larger doses of bismuth may solve the problem on a basis of efficiency, safety and ease holding. This, plus the growing promise of penicillin, offers hope of victory along these lines in the near future.

#### VALUE OF BISMUTH IN INTENSIVE SYSTEMS OF ARSENOTHERAPY

Clausen, Longley and Tatum,<sup>15</sup> on the basis of extensive studies in experimental syphilis on the coaction of bismuth and arsenic, reached the following conclusions. "Since the therapeutic coactions of bismuth and arsenical compounds are completely additive while their cotoxicities

are less than additive, there results a great margin of safety when they are used concurrently than when either is used alone in corresponding effective doses." Elsewhere in the article it is stated that "it would seem entirely justifiable to propose the administration of relatively large doses of bismuth concurrently with large doses of the arsenical within a period of a few days." Recent clinical observations are bearing out these claims.

Since bismuth has been used in conjunction with arsenic in the ambulatory intensive schedules employed in the Detroit Social Hygiene Clinic, we have no comparative figures. However with the Detroit plan of five day rapid drip treatment with oxophenarsine hydrochloride, the addition of bismuth greatly improved the results. Patients in the first half of our series were treated with oxophenarsine hydrochloride alone. Three injections of an oil-soluble bismuth preparation<sup>16</sup> containing 100 mg of metallic bismuth per dose were added on the first, third and fifth days of the intensive course to the latter half (200 patients) of our series. Satisfactory results were secured in 92.4 per cent in this series, compared with 70.4 per cent in the group not receiving bismuth. Conversely, there were 12.8 per cent of clinical relapses among those not given bismuth and none among those who did get it.<sup>17</sup>

Rattner,<sup>18</sup> in reporting his results with five day intensive therapy, stated that he had 86 per cent satisfactory response in 310 patients treated with oxophenarsine hydrochloride alone and 95 per cent satisfactory response in 111 patients receiving bismuth in addition. It is necessary, as Tatum<sup>15</sup> has emphasized, that the bismuth be used along with the arsenic for coaction and additive effect and not as a follow-up treatment. In short intensive systems (one to ten day) the amount of bismuth used during the period of arsenic therapy has probably not been sufficient to secure maximum benefit.

The announcement by Eagle (previously mentioned) that with arsenic alone he and his associates had 30 per cent of failures and only

15 Clausen, N. M., Longley, B. J., and Tatum, A. L. Quantitative Nature of the Coaction of Bismuth and Arsenical Compounds in the Therapy of Experimental Syphilis, *J. Pharmacol. & Exper. Therap.* **74** 324-333 (March) 1942.

16 Lipo-Bismol (Parke, Davis & Company)

17 Shaffer, L. W. Present Status of Intensive Arsenotherapy of Early Syphilis, *Ven. Dis. Inform.* **24** 108-113 (April) 1943.

18 Rattner, H. The Treatment of Early Syphilis by the Concurrent Administration of Arsenic (Mapharsen) and Bismuth in a Period of Five Days, *J. A. M. A.* **122** 986-989 (Aug. 7) 1943.

9 per cent of failures when one injection of bismuth subsalicylate per week was added still further confirms Tatum's coaction theory. More investigations need be carried out on the rate of excretion and blood levels of bismuth during treatment with various preparations of bismuth and on the maximum tolerated dosage for human beings.

#### CONCLUSIONS

1 Intensive arsenotherapy by intravenous drip, syringe technic, multiple injection or fever therapy plus arsenicals has proved satisfactory as far as end results are concerned.

2 A morbidity rate of 1 per cent and a mortality rate of 0.3 per cent from toxic encephalitis have caused the five day intravenous drip and multiple syringe methods to be looked on with disfavor.

3 There is hope that intensive schedules with smaller doses of arsenic (800 to 1,000 mg.) given over an eight to ten day period plus larger dosage of bismuth may prove decidedly safer and equally effective.

4 Results of treatment from fever therapy plus arsenicals are favorable, but the methods are technically too difficult for widespread use.

5 Ambulatory intensive treatment of the Eagle type offers the greatest promise for general use because of its safety, simplicity and equally effective results.

6 Eagle has stated, on the basis of the results obtained in the treatment of 4,800 patients in the cooperating clinics, that with three injections of oxophenarsine hydrochloride and one injection of bismuth subsalicylate per week continued for eight to ten weeks one may anticipate approximately 90 per cent clinical and serologic cures in cases of early syphilis.

7 Experience in the Detroit Social Hygiene Clinic with arsenic-intensive treatment schedule of both the five day and the ambulatory type indicates that the prognosis for early syphilis treated intensively depends on the duration of the disease.

8 The weakness of ambulatory intensive treatment is inability to hold clinic patients to schedules without lapse. A modified short hospital plan is desirable. Combinations with penicillin may supply this need.

9 Recent clinical observations are bearing out the claims of Tatum and his co-workers as to the effectiveness of bismuth in intensive schedules.

# INTENSIVE TREATMENT OF EARLY SYPHILIS WITH OXOPHENARSINE HYDROCHLORIDE BY MULTIPLE INJECTIONS

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The necessity for more rapid and more complete control of the contagious stages of early syphilis has been realized by every one familiar with the disease. The prolonged courses of treatment are tiring to patient and physician alike, and in these circumstances it is not to be wondered at that many far too many patients discontinue treatment long before the therapeutic possibility of cure is accomplished. Thus, inadequately treated patients are found in a large percentage of cases of early syphilis, and considerable evidence is at hand that inadequate treatment leaves the patient in a much less secure position than if he had no treatment at all. The natural immune developments take charge in untreated patients and attenuate the progress of the disease in many instances.

Great enthusiasm greeted the announcement of the results of treatment of early syphilis by a new method, first employed by Chargin, Leifer and Hyman in 1933.<sup>1</sup> These investigators, through various carefully controlled experiments with different arsenicals over a period of years, came to the conclusion that the continuous intravenous drip method of administering oxophenarsine hydrochloride (mapharsen) was highly curative. They realized the long time which must elapse in the course of such an infection as syphilis before definite conclusions could be drawn concerning any new form of therapy. They eagerly sought confirmations of their observations by other workers, and it was not long, therefore, before various groups began similar studies. Evan Thomas, of New York, was among the first to simplify the original method by the use of multiple injections, and he claimed results equally good.

Stimulated by these experiments and under the direction of Prof. Duncan Graham, of the Uni-

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<sup>1</sup> Chargin, L., Leifer, W., and Hyman, H. T. Studies of Velocity and Response to Intravenous Injections, J. A. M. A. 104: 878 (March 16) 1935.

versity of Toronto, we undertook the following study.

The method followed throughout was that of the treatment of patients with early syphilis by multiple injections, two injections of 100 mg. of oxophenarsine being given daily for a period of six days. The investigation was begun in May 1940 and has continued since that time. From more than 250 patients sent into the wards of Toronto General Hospital for this treatment, 206 were especially selected for treatment. Thirteen were given repeat or second courses.

Preliminary investigation before the beginning of the treatment included a thorough physical examination, together with many laboratory tests, such as dark field examination, Wassermann test, urinalysis (including tests for urobilin), van den Bergh test, hemoglobin determinations, white and red blood cell counts and estimation of nonprotein nitrogen. During treatment the urine was examined for urobilin every other day, and before the patient's discharge from the hospital Wassermann and van den Bergh tests were repeated.

The usual classification of early syphilis was followed: group A, seronegative primary syphilis, group B, seropositive primary syphilis, and group C, secondary syphilis.

After being treated in the ward, the patients were referred to the outpatient clinic for observation and follow-up, unless indicated, further treatment was not given.

## GROUP A—Seronegative Primary Syphilis

|   |    |
|---|----|
| Observed twelve to forty months               | 22 |
| Probably cured                                | 20 |
| Treatment failed                              | 2  |
| Observed less than twelve months              | 17 |
| Total number of patients treated              | 39 |
| Total number of cerebrospinal fluids examined | 18 |
| Total number negative for syphilis            | 18 |

Group A (seronegative primary syphilis), totaling 39 patients, shows probable cures of 20 observed over a period of twelve to forty months who had neither a clinical nor a serologic recurrence. For 2 other patients with a long observation period the treatment was considered a failure, though the possibility of a second



infection is present in 1 of these. Seventeen other patients in this group are not considered because the follow-up periods lasted less than one year. Eighteen of the patients in the group submitted to spinal puncture, and all reactions were negative.

#### GROUP B—*Seropositive Primary Syphilis*

|   |    |
|---|----|
| Observed twelve to forty months               | 32 |
| Probably cured                                | 26 |
| Treatment failed                              | 6  |
| Observed less than twelve months              | 53 |
| Total number of patients treated              | 85 |
| Total number of cerebrospinal fluids examined | 36 |
| Total number negative for syphilis            | 36 |

Group B (seropositive primary syphilis), totaling 85 patients, shows probable cures of 26 patients observed over a period of twelve to forty months. For 6 patients the treatment was considered a failure, and 53 patients cannot be considered because the observation periods lasted less than twelve months. Thirty-six spinal fluids were examined in this group after treatment, and all reactions were negative.

#### GROUP C—*Secondary Syphilis*

|   |    |
|---|----|
| Observed twelve to forty months   | 47 |
| Probably cured  | 39 |
| Treatment failed  | 8  |
| Observed less than twelve months  | 35 |
| Total number of patients treated  | 82 |
| Total number of cerebrospinal fluids examined   | 42 |
| Total number negative for syphilis  | 40 |
| Total number positive for syphilis (of which one became negative after further treatment) | 2  |

Group C (secondary syphilis), totaling 82 patients, shows probable cures of 39 and failure in treatment of 8. Thirty-five other patients cannot be included in the results because of insufficient observation (less than twelve months). Forty-two spinal fluids were examined in this group, of which 40 reactions were negative and 2 were positive. One of these fluids showing a positive reaction has since become negative with further treatment, and in the other instance the patient has been lost sight of.

#### SUMMARY (GROUPS A, B AND C)

Leaving out all patients who have been followed for less than twelve months, one may state with some confidence that those patients followed for from twelve to forty months in whom there was no clinical or serologic recurrence were probably cured.

It is not the purpose of this paper to deal with minor reactions, such as pain in the arms and chest after the injection, slight variations of urobilin or slightly abnormal results of clinical

tests, except to say that little technical difficulty was encountered and that laboratory findings on the whole were within normal limits.

Of the 206 patients treated, 13 had a second course of treatment. Eight seemed to be cured with this second course, but 5 did not so respond. The number of mucocutaneous recurrences in the entire series was 7.

The severity of reactions in this type of treatment makes its general use a doubtful procedure, and we regret to report 1 death from hemorrhagic encephalitis resulting from treatment. The following notes bear on this fatality resulting from treatment.

Y W, a 23 year old Chinese man, was admitted to the hospital on May 4, 1943, with a primary sore, a positive result of a dark field examination and a weakly positive Wassermann reaction. Physical examination showed nothing abnormal except the penile sore and a slightly enlarged inguinal gland. Urinalysis showed the specific gravity to be 1.025, with no abnormal findings. Hemoglobin was 97 per cent and the white blood cell count 9,600, the indirect van den Bergh test showed 0.8 units.

On May 10, after the patient had had a ninth injection of oxophenarsine hydrochloride, a slight fever developed. The next day his temperature was 101 F, and the morning injection was omitted. It was decided to finish the course, and he was given his last dose at 9 a. m. on May 12. On the evening of May 12 the patient had a convulsion, fell to the floor and was unconscious. The next morning he was still unconscious. The eyes were strongly deviated to the left. The head was somewhat retracted and resisted flexion but was not stiff. The patient was unresponsive to a pinprick. The right arm and leg seemed more flaccid than the limbs on the left side. Tendon reflexes were present and active. The right plantar reflex was of the extensor type and the left flexor. The pupils were moderate in size and reacted to light. The fundi could not be seen well, and there was no gross papilledema and no hemorrhage. On the evening of May 15, the patient had another convulsion, lasting two minutes. He had a temperature of 103 F. There were no further convulsions but the patient died that night.

A lumbar puncture was made on May 13, the fluid was clear and the pressure was 190. The Queckenstedt test showed a slow rise and a slow fall. There was a trace of a Pandy reaction, there were 33 cells. The Kolmer-Wassermann reaction was partially positive, the chlorides were 740 mg per hundred cubic centimeters.

Death was thought to be due to toxic encephalopathy following treatment with oxophenarsine hydrochloride, though permission for autopsy could not be obtained.

Other reactions of some importance in this series occurred in 2 patients with ocular complications.

A D, admitted to the hospital in August 1941, with secondary syphilis, was given six days of treatment with oxophenarsine hydrochloride without incident. His Wassermann reaction of the blood became negative in eight weeks. In October he was admitted to the hospital with thrombosis of the right inferior vein of the right eye. There was a central scotoma and pronounced iritis. He suffered from severe acne rosacea, and the ophthalmologist's opinion was that the iritis might easily

have been due to his infection with acne. The sight has been permanently lost in this eye.

• M. W. was admitted to the hospital with a primary sore, a positive result of dark field examination and a positive Wassermann reaction. When eight treatments had been given—that is, when the patient had been undergoing treatment for four days—he began to complain of blurring vision. On examination, fine vitreous opacities were seen in both eyes. Both disks were somewhat blurred, but there was no definite edema. The visual fields were difficult to measure, but there seemed to be a small relative central and paracentral scotoma. Both maculas showed some stippling, suggestive of a degenerative lesion not associated with syphilis. The vitreous opacities might well have anteceded the syphilitic infection, according to a note of Jan 26, 1943. However, after this examination, the patient was given fever therapy, and both the disks and these vitreous opacities came definitely clearer. The patient's vision also improved.

The interesting reaction of Milhan's ninth day erythema was seen in 6 of our patients.

One of our patients (R. B.) was given treatment in March 1942 and remained free of syphilis, clinically and serologically, for one year. In April 1943, he married a known syphilitic, and some edema of the penis developed and his Wassermann reaction became positive. He was treated again and appears to have been cured clinically and serologically in twelve months.

Only 1 patient was treated during pregnancy. Treatment was well tolerated, and the baby was nonsyphilitic.

L. W., a woman aged 47, received treatment for extragenital lip chancre and secondary eruption in October 1942. Treatment was well tolerated, but a month later jaundice was noted. This was thought to be of arsenical origin, but on her admission to the hospital in January 1943 an exploratory laparotomy showed a carcinoma of the gallbladder with secondary nodules in the liver. No attempt was made to remove the growth, and she died a month later. Her Wassermann reaction, tested on two occasions when she was in the hospital, was reported doubtful and weakly positive.

#### THE INTENSIVE TREATMENT OF SECONDARY SYPHILIS WITH OXOPHENARSINE HYDROCHLORIDE BY MULTIPLE INJECTIONS

The experimental work of Eagle and Hogan<sup>2</sup> with syphilis in rabbits suggested that tolerance to large doses of arsenic was dependent, at least in part, on the length of time over which it was given. In this work they suggested that even larger doses should be given over periods of weeks rather than days, thereby lessening the risk of toxic reactions without lowering the chances of probable cures. Among the schedules of treatment suggested was that of injecting oxophenarsine hydrochloride (1 mg per kilo-

gram) three times weekly for five to ten weeks. Eighteen months ago it was decided to treat patients in the secondary stage of syphilis by a course of three weekly injections of oxophenarsine hydrochloride (40 to 60 mg) for ten weeks and one injection weekly of bismuth (0.2 Gm) for the same period.

#### Secondary Syphilis

|  |          |
|--|----------|
| Observed nine months   | 30       |
| Probably cured   | 24 (80%) |
| Treatment failed   | 6        |
| Total number of cerebrospinal fluids examined                                | 11       |
| Total number negative for syphilis (From patients probably cured)            | 9        |
| Total number negative for syphilis (From patients for whom treatment failed) | 2        |

All patients chosen were in the secondary stage of syphilis and some had had their infections for many months. Forty-seven patients commenced treatment, but since they were outpatients 6 did not complete their courses and were lost. In 1 patient a mild arsenical dermatitis developed, and treatment was stopped. The rest of the group have had less than nine months' observation. The almost complete freedom from reaction of any kind, even though the treatment is intensive, suggests that this plan may be a compromise between the short and the prolonged treatments. We suggest, however, that all patients be hospitalized during the entire treatment to insure its completion.

#### ABSTRACT OF DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich. There is a great deal of misconception, certainly among the laity and to a certain extent among practitioners, as to just what the purpose of the rapid treatment program for syphilis is as it has been initiated and carried out by the United States Public Health Service.

This is not an attempt to find a cure for syphilis. No form of rapid treatment which applies only to early syphilis or to primary, secondary and early latent syphilis can in any way be regarded as a cure for syphilis as a whole. There is no rapid treatment measure applicable as yet, unless one includes penicillin, to the late stages of syphilis or to the various forms of syphilitic systemic disease.

The problem initially was this. There was every reason to suspect from experience in the last war that there would be a tremendous increase in the incidence of syphilis in the civilian population, which would definitely reflect itself in the armed forces. The cost of syphilis and the other venereal diseases in soldier hours is something that mounts into stupendous figures.

For this reason the campaign was initiated through the appropriation of the United States Senate and House of Representatives, which set aside some \$300,000,000 for the welfare of the peoples of the various communities and states which were not able to finance such enterprises or such projects themselves. In this welfare program, the control of venereal disease in the lay population was considered as an appropriate and proper component.

<sup>2</sup> Eagle, H., and Hogan, R. B. Intravenous Drip and Other Intensive Methods for Treatment of Early Syphilis, *Science* 95:360 (April 3) 1942.

The states were encouraged to apply for federal funds to establish, through state agencies, rapid treatment centers for the treatment of infectious venereal diseases. In states which were unwilling or unable to so operate, the federal government was willing to do so.

It was proposed to isolate in these rapid treatment centers patients with communicable gonorrhea, syphilis and chancroid during the period of their infectiousness and during this period to institute such treatment as would render them incapable for the most part of communicating their diseases when they were released. That is the project in a nutshell.

To date there have been established some forty-eight of these rapid treatment centers in various parts of the United States and of the Caribbean area, with a total of something like six thousand five hundred beds.

There is some objection—I think legitimate objection—to all rapid treatment methods. The first objection I have is that it is not good medical practice, except in a time of national emergency. There is nothing, I believe, that requires more individualization than the appraisal of a patient with syphilis. When one lumps them all together and decides that one is going to initiate some specific type of treatment, the individual is necessarily sacrificed to the whole group. The second objection is manifest in the present discussion. The condensation of a treatment program, which with conventional treatment occupied from eighteen months to two years, into a period of a few days or two weeks materially increases the toxic reaction incident to the drug.

I believe, however, that these shortcomings find their justification in the fact that during this period there have been placed under observation for a period of several weeks, sometimes as many as twelve weeks and seldom less than a month, patients who were in the communicable stage of venereal diseases, and they have been treated to the point where they were probably unable to infect others.

The follow-up has been such that one can be reasonably sure that the majority of them have been rendered non-infectious.

The sole objection to the multiple syringe injection that Dr Shaffer is using, a modification of the Eagle method, is that this is not a hospital procedure. Patients so treated in an outpatient department are still capable of infecting others while they are footloose and outside the hospital ward. The therapeutic results of this method compare favorably with those of other rapid treatment methods in use.

Another justification, I think, for rapid treatment methods, if one seeks for additional justification, is this. It has been shown in dispensary practice that under the best conditions about 30 or 40 per cent of patients with infectious syphilis will take sufficient treatment to render themselves noncommunicating, then they are lost. In any form of rapid treatment that is being employed, whether it is one day treatment with fever and oxophenarsine hydrochloride or the five day drip or the Schoch method or the modified Schoch treatment which Dr Trow has just reported on, the patients get all their treatment in a short time and the matter of case holding ceases to be as important as it would be in ambulatory dispensary treatment.

With regard to the fatalities, one may really be surprised that there have been so few in the circumstances in which rapid treatment has been carried out in the United States Public Health Service and in the armed forces. A few of the officers are trained in venereal disease control, and a smaller number can be said to be qualified venereologists. Many of the ablest officers have been pediatricians, internists, neurologists and gen-

eral practitioners, and not a few have been recent graduates with but one year of internship service. Those allocated to this division have had refresher courses of instructions, and to my way of thinking it is remarkable that they have done so well with the various methods used. They are handicapped not only by insufficient training but by inadequate staff and nursing assistance.

Rapid treatment methods under existing conditions are not to be recommended at this time for general medical use. The reason is obvious from the previous statement. It is hoped that within a few years, or better, a period of a few months, such methods may be abandoned in favor of the rapid treatment method now being undertaken with penicillin.

In the whole group there has been an incidence of some 0.3 per cent of fatal encephalopathy. I believe that that is being cut down materially at the present time.

In perhaps a third of the centers an eight day program has now been instituted, and to date over 1,000 patients have been treated with no fatalities. Moreover, the officers have learned when to stop and when the contraindications or indications are present for cessation of treatment.

I do believe (it was brought out before in the discussion of Dr Eagle's method) that many of the patients who have died of the treatment could have been saved had the observers been more experienced.

DR HAROLD N. COLE, Cleveland. I was much interested in Dr Shaffer's paper. Dr Shaffer has been one of the most active men in the United States, I think, in this problem of intensive treatment.

In Detroit, Cleveland and many others of the large cities, the enormous influx of Negroes has created a real difficulty, since from 35 to 40 or 50 per cent of the cases of syphilis occur among these people. They are difficult to handle, they may take a few treatments and disappear from observation, as Dr Wile has said.

It is on that account that I agree with Dr Wile that these patients must be hospitalized and that they must receive all their treatments while they are in the hands of the physician. If he does not give it to them then, they will never get it. There will be only about 30 per cent of the patients that will finish their treatments with any ambulatory form of treatment. No matter how careful one's follow-up and how perfect one's organization is, there will still be difficulties.

Major Roy Kile, of the United States Public Health Service, formerly in practice in Cincinnati, is in the Cleveland area. He has done a wonderful job and has aided tremendously in carrying on the work along this line.

I have just looked over this paper of Dr Shaffer's and noted a few salient points. With the Eagle method of treatment that was carried on by the ambulatory method, of 352 patients, 194 did not complete their treatments. They received a few injections and were feeling good, and Dr Shaffer, despite the organization he has built up, was unable to find them. That is what it amounts to.

With his other plan of ambulatory intensive treatment that he used in Detroit, which is a good plan, he did succeed in getting 63 of his 210 patients to complete their treatments.

In the Cleveland area there is a hospitalization plan at the City Hospital and at the University Hospitals, and patients are put in the hospital and given their treatments and then allowed to go out. One will lose a good many of them afterward but one knows they have had their treatments at least.

I have been employing the Thomas

My associates and patient a daily injection of an arsenical, giving three, with a treatment on the second, fourth, sixth and eighth days of typhoid paratyphoid fever. Usually the temperature will go down and the method have worked out well. One must watch these patients carefully. If one does not have a trained or unable to carry every patient through to the end of the treatment. I believe, however, that this method of therapy that is available today and that it results in about 90 per cent of cures. When the patient has left the hospital, one knows that he has had his treatment and that, by and large, it will be satisfactory.

There are now many Negroes coming to the two centers in Cleveland asking for the rapid treatment for syphilis. Of course, the rapidity of treatment will constitute one advantage of penicillin, and it may be that the use of penicillin will supplant this intensive treatment with the Thomas-Wexler method. But, certainly in wartime, with the problem that exists in connection with the Negro population, the hospitals must have beds for these patients and they must be given intensive therapy, if anything is to be done toward solving the problem of syphilis.

DR CHARLES C DENNIE, Kansas City, Mo. Is the arsenical given after the fever is beginning to drop?

DR HAROLD N COLE, Cleveland. The arsenical is given as nearly as possible at the height of the fever.

In this connection, I might mention that bismuth therapy is also given. In the City Hospital such patients have been given three injections of bismuth subsalicylate. At the University Hospitals they have been given five injections of bismuth. There have been between 200 and 300 patients treated by this method.

DR EARL D OSBORNE, Buffalo. Independently I have come to exactly the same conclusion as Dr Cole has about his rapid treatment. Any physician in a large city with a floating population, including sailors and Negroes, has to hospitalize such patients. With the best system of follow-up, one cannot successfully treat more than one third of those patients in a large city.

Another plan I have used for some time is to follow up with bismuth. This plan has the advantage of keeping the patients under observation, if no other.

I thought Dr Wile would mention something about the deaths. When he was in Buffalo a year or so ago, he asked me about deaths. I said I had had 1 death and 1 near fatality. Immediately he asked if these were women and if the women were menstruating. The woman who died was a healthy nurse and was menstruating when the treatment was started. The other patient, who almost died, was a man who had his five day treatment, went home and immediately went on an alcoholic debauch.

As Dr Wile pointed out, menstruation and alcoholism are definite contraindications to any intensive arsenical therapy.

DR PAUL A O'LEARY, Rochester, Minn. About a year and one-half ago I was asked to come to Chicago and set up a program for the Chicago Intensive Treatment Center. The one day treatment with fever therapy and chemotherapy has been in use for twenty months, and up to date about 1,300 patients have been treated by this method, of whom 4 have died. They died of

shock, primarily heat shock. As far as completion of treatment is concerned, this is certainly the ideal method because it is given in one day, although three days are required from the time patients enter until they leave the hospital. Contrary to the general impression, the successful results up to the moment have been about 55 per cent, or, in other words, there has been a known failure incidence of 45 per cent in the year and one-half follow-up of a large group of patients.

It was thought advisable to establish comparable systems of treating early syphilis, not only because there was a vast amount of material available but because some patients were not eligible for the one day plan and it seemed advisable to utilize other systems as well. Accordingly, the Schoch system, three injections of oxophenarsine hydrochloride a day for ten days, and a modified Eagle system, injections of oxophenarsine hydrochloride three times a week and of bismuth twice a week for eight weeks, were adopted. It was planned to give a minimum of 1,200 mg of oxophenarsine hydrochloride in a period of eight weeks, with a comparable amount of bismuth.

The Schoch system was used for some 500 patients, of whom 300 completed the course. The successes with the Schoch treatment were about 50 per cent, but such complications as facial edema and fever occurred in approximately 18 per cent of the patients.

With the Eagle system, 515 patients with acute syphilis were started on treatment, of whom 173 completed the course. Only 33 per cent of them completed the course, even with the inducement of free room and board.

The intensive treatment of early syphilis is in a state of confusion. Every one has a system of his own, with the result that it will be many years before one knows the ideal program. In fact, the best intensive plan may never be known because penicillin is apparently going to produce just as satisfactory results in a shorter time with few unfavorable sequelae. In fact, the best results noted thus far in my experience in the treatment of early syphilis are seen in those patients who receive a short course of oxophenarsine hydrochloride followed by 1,200,000 units of penicillin and then by another course of oxophenarsine hydrochloride.

The program for treatment of acute syphilis is far from settled. As one studies the charts showing the results in the treatment of early syphilis, one is surprised to discover that most workers report satisfactory results in approximately 85 per cent of the cases. This is true of the "good systems," whether given over an eight week or an eighteen month period. Accordingly, it would seem advisable to spend some effort in trying to determine what is wrong with the 15 per cent who seem to fail to obtain a "cure" irrespective of the system employed.

DR A BENSON CANNON, New York. I enjoyed the paper by Dr Shaffer and the one by Dr Trow and Dr Dixon. Dr O'Leary's discussion was excellent and to the point.

I believe with Dr Wile and Dr Cole that the ideal method of treating a syphilitic patient or a patient with almost any disease, for that matter, is by hospitalization. On the other hand, it is not practical to hospitalize every syphilitic patient for treatment and I am convinced that no method of treating syphilis can ever be universally successful that cannot be applied to ambulatory patients. Hospital facilities are not adequate, the expense is too great, social and business reasons make it impractical for one to confine a patient to a hospital for the purpose of this treatment. I believe that it is necessary to have

more than one plan of treatment. There should be one for the persons with early syphilis who can be hospitalized for treatment given intensively for short periods. There should be another one, a bit less intense, for patients who can be kept in the institution for two or three weeks, and, finally, one or two other plans that will be still less intense than the others and will meet the requirements of the office and clinic patients.

In 1924 and 1925 I was able to observe the records of 800 patients with early syphilis treated by Dr. Kyle of Vienna with a course of neorasphenamine followed by one of malaria. I was so impressed with the good results that he had obtained that I started a similar treatment of the patients at the New York City Hospital in 1925 and continued that method until three years ago. Since that time, I have used a twelve day treatment with malaria in combination with bismuth, and so far there have been no fatalities and the results have been good. I have treated patients in the clinic with daily injections of oxophenarsine hydrochloride and another group with daily injections of old arsphenamine in combination with bismuth, completing the treatment within seventeen to thirty days. I am convinced that any quick cure of early syphilis with arsenic must be reinforced with bismuth, or perhaps with fever therapy, to be most effective. Not only does one obtain a greater percentage of cures when giving the bismuth in conjunction with arsphenamine, but one is also able to prevent mucocutaneous recurrences, provided that the bismuth is given frequently enough and in large enough doses over a sufficient period.

Reactions are surprisingly few considering the intensity of the therapy. Among 100 patients treated daily with oxophenarsine hydrochloride (12 to 136 mg) there was only one serious reaction, 1 patient after the ninth injection became semiconscious and had several light convulsions, over some eight hours' time. The disappearance of the reaction was as quick as the onset, the patient suddenly awoke remembering nothing and feeling all right. I have just been told of a second case, that of a young Negro girl admitted to the Presbyterian Hospital with granulocytopenia three weeks after being discharged from the New York City Hospital, where she had completed her treatment. It is probable that other similar cases of severe delayed reactions following the intensive arsenotherapy have been observed by others, especially of mucocutaneous relapses following intensive arsenotherapy. In the last three years I have observed 6 patients with mucocutaneous recurrence of syphilis who had been followed for a year or longer and reported cured by another institution.

I think it is clear from Dr. Shaffer's paper and also from that of Dr. Trow and Dr. Dixon that the greater the amount of an arsenical one gives in the shortest length of time the more reactions one observes and the more serious are the complications.

I believe with Dr. Cole, Dr. Trow and others that any plan of treatment in which one can give the minimum amount of arsenic and produce the maximum number of cures is a highly desirable one. But, as Dr. O'Leary has just brought out in his discussion, we all recognize that probably the minimum effective total amount of oxophenarsine hydrochloride is something like 12 Gm., hence, I think that one is expecting a great deal from four injections of typhoid vaccine if they have to make up for the deficit in the arsenic. I cannot help feeling that the 0.7 mg of oxophenarsine hydrochloride and the four injections of typhoid vaccine are insufficient to treat a patient with early syphilis, and I suspect that the advocates of the method

will encounter a great many infections. I have been recent graduate nursing service. Those long periods of observation had refresher courses of

Dr. Shaffer, Dr. Trow and Dr. Dinking it is remarkable some especially fine work, and I am sure the various methods results will prove to be most valuable, only by insufficient of syphilis, even though the new curative nursing assistance cillin is available ing conditions are

DR. NORMAN N. EPSTEIN, San Francisco. I have been interested in the subject of the intensive treatment of early syphilis for a considerable period. For a period of however, accumulate such large numbers of cases in favor of early syphilis for study in San Francisco as have been taken with reported here. After the first reports on the five year treatment showed that this procedure was too toxic for general use and after Thomas showed that with a total below 900 mg of oxophenarsine hydrochloride given by this intensive method serious toxic reactions did not occur, I thought that perhaps the addition of fever therapy to a program of intensive treatment would permit a reduction of the dose to safer limits for two reasons. First, artificial fever itself has a spirocheticidal effect provided the particular tissue invaded by the organism can be raised to a temperature of 105 or 106 F. Second, artificial fever seems to enhance the therapeutic activity of oxophenarsine hydrochloride. It seems, however, to increase the toxicity as well.

Therefore, using my method of fever therapy, I administered 840 mg of oxophenarsine hydrochloride in a period of eight days, combined with three sessions of artificial fever of five hours each, the temperature being elevated to 106 F.

The twenty-fourth patient, at the completion of his treatment suddenly lost the use of both legs. He had bilateral paraplegia due to severe myelitis. This patient had received only 840 mg of oxophenarsine. The dose was therefore reduced to 720 mg. This group of patients, although small in number, has done well.

The effect of oxophenarsine hydrochloride on *Treponema pallidum* can be studied clinically in cases of arsenic-resistant syphilis. I had 3 such patients referred to me for this intensive method of treatment, and in each one the lesions disappeared promptly, showing that even this small amount of oxophenarsine, when supported by three episodes of sustained fever, increases in therapeutic efficacy. I believe that the development of myelitis in 1 of my patients indicated that the toxicity of the drug is increased too. The introduction of so many different methods for the intensive treatment of syphilis has led to considerable confusion, which should be clarified as soon as possible.

DR. UDO J. WITF, Ann Arbor, Mich. How is the fever induced?

DR. NORMAN N. EPSTEIN, San Francisco. The fever is induced simply by wrapping patients in blankets. This procedure has been described under the title "The Blanket Method of Inducing Artificial Fever."

DR. JOHN G. DOWNING, Boston. Nowadays I am rather sorry for the authors who have written books on the treatment of syphilis. This year when a student asked me what book to buy on the treatment of syphilis, I said, "Wait another week." The thought that occurs to me about all these rapid treatments is that we are still forgetting that nature is the best physician. We are still forgetting the possibility of building up a natural immunity. I think that oversight has been brought out by the close follow-up at one of the clinics that I am attending. The Eagle treatment was introduced at that clinic at the very onset. The patients were treated in the hospital and were given their complete courses in from eight to twelve weeks.

My associates and more patients with dark field-method, giving the syphilis have had serologic relapses arsenical for ten or whom treatment was started when fourth, sixth and serologic reaction. Perhaps these revaccine intraveno the extreme sensitivity of the Hinton perature will give

results of this W. SHAFER, Detroit. First, I wish to watch these appreciation to all the discussants for the trained or shown in these papers. There are a number of will be I should like to have had time to discuss more conclusively and which I discussed in greater detail in this paper.

method point that Dr. Trow brought out in his paper, will I possibly should not discuss, was the fact that patietically all the reactions in the spinal fluid were hadative. The same result has occurred in my own experience, and it has been rather surprising to me.

In a total of approximately 700 examinations of spinal fluid, made usually at the start of treatment so that the effect of treatment could not be given as the reason for the negative reaction, I have found only 28 positive reactions (4 per cent), a figure which certainly does not agree with the literature on the question of the incidence of positive reactions in the spinal fluid in early syphilis. I have no explanation for it.

I should also like to mention the question of treatment of relapse. In most articles on intensive therapy, the statement is made that in general the results of treatment of relapses were as satisfactory as those of treatment of original cases. This statement does not agree with my experience. I think that such results could hardly be expected. In my series of approximately 100 patients, when the patients were not cured with intensive therapy and were retreated satisfactory results were secured in only approximately 50 per cent of such patients.

The whole question in this discussion can well be summarized as follows. In the first place, short hospital methods of intensive therapy are indicated only for clinic patients who cannot be held without a lapse of treatment by the standard method. I would certainly not propose to use them in private practice.

Some one asked a while ago what I would do if I had it. If I had early syphilis, I certainly would not want to take a chance, nor would I want to urge a patient who was perfectly cooperative to take a chance with intensive therapy. Its use is justified only for those patients experience with whom indicates that a high percentage will not complete the treatment or that it must be completed in a short period of time.

My experience with the Eagle method of treatment, although it is safer and although the end results compare favorably with the short methods of treatment, is that, again, one faces the insurmountable problem of case holding among these patients. Therefore, it is not satisfactory at least for the type of clinic patients that

one has in Detroit, and that I believe is representative of the type of syphilitic patient in any city where there is a large Negro population.

It is necessary to work out some short method of treatment with hospitalization. Further improvement certainly needs to be made in reducing the toxic effects of treatment. Possibly combinations of arsenic and bismuth with penicillin will solve this problem.

Dr. Osborne, after his discussion, said that he wanted to call attention to the figures that I cited in reference to the Thomas-Bellevue method, a combination of multiple injection plus typhoid, and that results cited in his printed reports were better than my statistics showed—in other words, better than 90 per cent. I have no statement to make on that. I quoted from the evaluation study of the United States Public Health Service, made from their own statistical department on the collected reports from the New York clinics and the midwestern groups. I can only accept them and hope, at least, that they are accurate. Incidentally, I did not have time to explain all of the various methods of treatment discussed in my paper.

I believe that Dr. Cannon's multiple injection method using arsphenamine was the last one quoted in that series. Incidentally, if I had time to go over the details on those slides, he would have seen that, next to the rapid treatment method with neoarsphenamine, fever therapy plus the multiple injection method gave the best results of any of the other methods listed in that evaluation.

DR. H. A. DIXON, Toronto, Canada. There is little I can add to what Dr. Trow has told you except these few points. The bismuth used was bismuth oxychloride, a water-soluble bismuth. There were 161 men and 45 women treated.

In the six day course, before treatment was started, 4 patients had 2 to 4+ reactions for urobilin. We were somewhat hesitant but went ahead, and the urobilin reactions were negative by the end of the six day course.

In 3 patients, the van den Bergh reaction was 1 unit to 2 units before the six day course was begun but were normal by the sixth day.

The Wassermann reaction became negative in an average period of five weeks after the course of treatment. I think that Chargin, Leifer and Hyman reported that the reaction became negative in an average period of twelve weeks after the course—that is, after use of the drip method. The results of the tests for hemoglobin were all 85 per cent and over.

The six day intensive, or multiple injection, course is still in the experimental stage. It is not suitable for general use. Patients must be in the hospital where they are under careful observation.

I wish to thank Dr. Wile and the other members for their interesting discussion of this paper.



# ONYCHOMYCOSIS AND DERMATOMYCOSIS CAUSED BY TRICHOPHYTON RUBRUM AND ASPERGILLUS NIDULANS

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To our knowledge, multiple infection of the nails with more than one species of fungus has never before been reported. The presence of a *Trichophyton* and an *Aspergillus* together is unusual in human tissue. Onychomycosis caused by the genus *Aspergillus* alone is extremely rare, in fact, the aspergilli have usually been considered, and often are, contaminants of mycologic cultures. There are only a few recorded instances of fungous infections of the nails attributed to the aspergilli and related fungi.

The first case reported was that of Émile-Weil and Gaudin,<sup>1</sup> in 1919. Sartory<sup>2</sup> reported a case in 1920 and Ota<sup>3</sup> another in 1923. Sartory and co-workers<sup>4</sup> reported another case in 1930. Smith<sup>5</sup> reported a case in 1934. From 1934 until 1941 no other cases were published.

In 1941 Bereston and Keil<sup>6</sup> reported the last case of aspergillosis of the nails to be found in the literature, and for the first time the organism concerned was found to be *Aspergillus flavus*. This organism was identified after having been isolated repeatedly, and its identity was confirmed by Dr. Charles Thom, principal mycologist, United States Department of Agriculture, since retired. A careful search of the literature since 1941 has revealed no further investigative work in this field.

1 Émile-Weil, P, and Gaudin, L. Onychomycosis causees par *Sterigmatocystis unguis*, Arch de med exper et d'anat path 28 465, 1919

2 Sartory, A. Sur un champignon nouveau du genre *Aspergillus* isole dans un cas d'onychomycose, Compt. rend Acad d sc 170 523, 1920

3 Ota, M. Sur une nouvelle espece d'aspergillus pathogene *Aspergillus Jeanselmei*, Ann de parasitol 1 137, 1923

4 Sartory, A, Sartory R, Hufschmitt, G, and Meyer, J. Un cas d'onychomycose provoquée par un *Eurotium* nouveau *Eurotium diplocyste* n sp, Compt rend Soc de biol 104 881, 1930

5 Smith, L M. *Aspergillus* Infection of the Nails, Urol & Cutan Rev 38 783, 1934

6 Bereston, E S, and Keil, H. Onychomycosis Due to *Aspergillus Flavus*, Arch Dermat & Syph 44 420 (Sept) 1941

Thom and Church<sup>7</sup> have criticized most of the case reports of aspergillus infection of the nails as well as of other tissues, on the ground that they lacked data on the careful identification of the cultures and that clinical information was often fragmentary.

In view of the extreme rarity of human infection with aspergilli, we felt that our present case was worthy of being reported. The fact that for the first time *Aspergillus nidulans* was isolated from a human patient with onychomycosis and that *Trichophyton rubrum* was also present added to its interest.

## REPORT OF A CASE

A white officer, aged 38, was seen by one of us (E S B) in an outpatient dermatologic consultation early in June 1944. He gave a history of having had no trouble with the skin until fourteen months previously, while stationed at an airfield in Alabama, when he first noticed a thickening of the nail of the left great toe. This lesion was followed several months later by a thickening of the nail of the middle finger of the left hand. Thereafter the nails of the right great toe and the index and little fingers of the left hand had also become involved. During the past six months the skin of the toes and soles of both feet had been scaling. The patient noticed that the affected nails became brittle and crumbled in their distal portions. He had previously received treatment with an ointment of benzoic and salicylic acid, without improvement.

On examination the skin of the feet and toes showed occasional vesicles and patches of superficial exfoliation, located chiefly on the plantar surfaces of both feet. The nails of both large toes were brittle, had a grayish green discoloration and were crumbling in their distal portions. The nails of the index, third and little fingers of the left hand were similarly affected but to a lesser degree than the toe nails (fig 1).

Scrapings of all nails were made and sent to the laboratory for direct examination and culture. A clinical diagnosis of onychomycosis of the affected finger and toe nails and of dermatomycosis of the feet was made. The patient was told to scrape the nails each day with the edge of a glass slide and to apply thereafter 10 per cent ammoniated mercury ointment. Castellani's solution was ordered to be applied daily to the affected skin.

7 Thom, C, and Church, M B. The Aspergilli, Baltimore, Williams & Wilkins Company, 1926



of the toes and feet. These treatments were carried out faithfully for two months. Roentgen therapy to the affected nails was instituted and was given in four weekly treatments to equal a total dose of 600 r with a 0.5 mm aluminum filter.

The patient was observed for a period of three months, and during this time the skin of the toes and feet cleared completely but the nails did not improve at all, and despite the treatment carried out, as will be shown subsequently, they still yielded positive evidence of fungi on direct and cultural examination.

**Laboratory Observations**—Scrapings of the affected skin and nails were taken with great care by scraping the surface material directly into sterile Petri dishes, in order to avoid contamination. These specimens were sent directly to the laboratory, where representative portions were inoculated into Sabouraud's dextrose agar, malt agar, wort agar and corn meal agar, according to the routine procedure of this laboratory. Ten per cent potassium hydroxide hanging drop slides were then prepared and examined directly and after standing overnight. The results of nineteen different samples taken over a period of two months are shown in the table. These specimens were taken only from underlying portions of the nails after the outer portions had been scraped away. The fungi found cannot therefore be

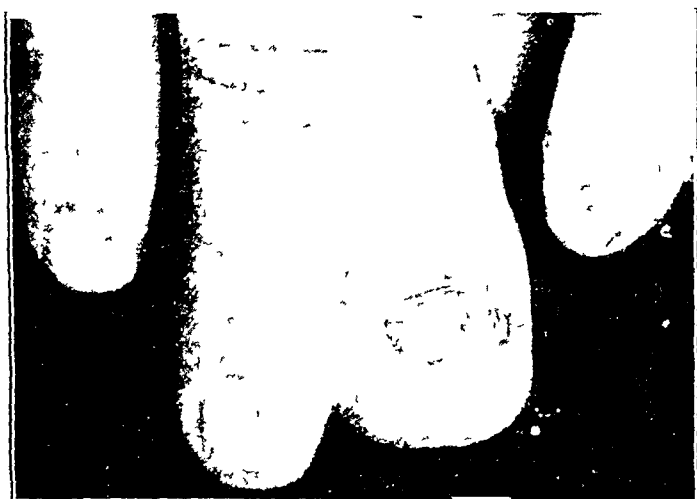


Fig 1—Characteristic appearance of onychomycosis of hands and feet

said to result from spores lying on the surface of the tissue. In addition, the patient was receiving roentgen ray and local therapy with fungicides during the entire two months of laboratory study. From the table it can be seen that of sixteen samples from the nails taken over a period of two months fourteen yielded positive evidence of fungi on direct microscopic examination in 10 per cent potassium hydroxide solution after standing twenty-four hours. Three samples of skin from the feet, taken two weeks apart, were all positive for fungi on direct examination and on culture. Forty of the sixty culture tubes inoculated with specimens of the affected tissues (skin and nails) yielded the species of *Aspergillus*. Forty-nine of the sixty cultures yielded in addition a species of *Trichophyton*. Twelve tubes inoculated with specimens from unaffected nails, as controls, yielded no growth.

Direct microscopic examination of the affected nails in a large number of the positive specimens examined showed two separate and distinct types of mycelium: one, the thin *Trichophyton* type, the other, the thicker *Aspergillus* type.

The cultures on the four types of mediums employed showed two separate types of fungus growth (fig 2).

Three to five days after inoculation and incubation at room temperature there appeared a slight grayish mycelium which in a few days became a light green fluffy colony with yellow and greenish powdery spores on the surface. This was considered to be an *Aspergillus*. One to two days after the appearance of the *Aspergillus* a white cottony growth also appeared in the culture tubes. This was identified as a species of *Trichophyton*.

Samples 11, 12 and 13 were controls taken from what appeared to be unaffected nails and were negative for fungi on culture, although on direct examination one specimen showed septate hyphae.

Specimens of the two organisms which were isolated were sent to Dr C W Emmons, principal mycologist, United States Public Health Service, National Institute of Health, Bethesda, Md, for exact identification. He identified them as *T. rubrum* and *A. nidulans*. Dr Emmons stated that he felt the *Trichophyton* to be the cause of the onychomycosis and that the *Aspergillus* was either a contaminant or a secondary invader in already diseased nails.

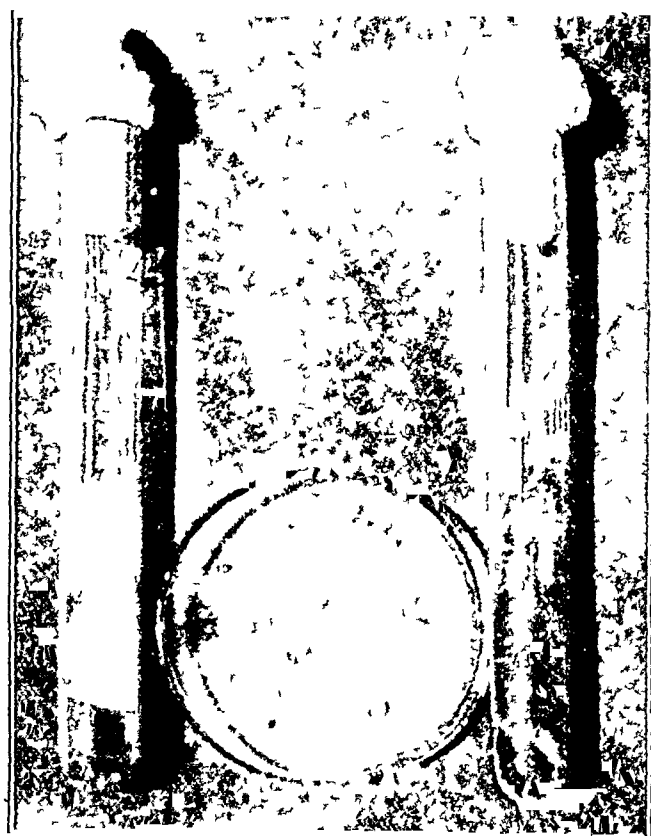


Fig 2—The tube on the left shows a culture of *T. rubrum*, the tube on the right, a culture of *Aspergillus nidulans*. Both organisms can be seen growing on the Petri dish. (Official photograph, Signal Corps, United States Army, from the photographic laboratory, WSCTC, Camp Kohler, Calif, no 9SC-44-K-969)

#### COMMENT

This case is of particular importance not only because of the multiple infection but because of the fact that one of the organisms, *A. nidulans* has never been reported before as a cause of human onychomycosis. Swartz<sup>8</sup> mentioned that an *Aspergillus* related to *A. nidulans* has been found in a mycetoma of the black-grained type.

8 Swartz, J H. Elements of Medical Mycology, New York, Grune & Stratton, Inc, 1943, p 153.

Onychomycosis due to the species of *Trichophyton* is common, but we wish to point out the fact that aspergilli can be a cause of human onychomycosis, either alone or in combination with other species of fungi

In the present state of knowledge, aspergilli are considered by most mycologists to be cultural contaminants, although, as has been stated, the literature records examples of pathogenic infection of human tissues with these organisms

The fact that each time that the *Aspergillus* appeared in our cultures it appeared simulta-

hood that the *Aspergillus* was a contaminant on fifteen separate occasions

A clinical feature observed by one of us (E S B) in a case of onychomycosis due to *A. flavus*<sup>6</sup> was the greenish discoloration of the involved nails. This greenish deep-seated discoloration of the nail plates was also seen in the present case. The discoloration in this case is believed to be due to the growth of the *Aspergillus* in the nail plates. *Trichophyton* infections of the nails do not show this distinctive discoloration.

The rarity of superficial aspergillosis raises the question as to what weakness in tissue resistance or abnormality of metabolism in the host permits the initial growth of these fungi. It would certainly appear that the normal human body is naturally resistant to such omnipresent fungi as the aspergilli. In the case reported here—it is possible that the common pathogen *T. rubrum* was the primary invader, lowering tissue resistance for a secondary invasion of the apparently less pathogenic *Aspergillus*. If this is true, it would be likely that there are more of such multiple mycoses than are reported. This might be explained by the fact that many mycologic laboratories, as mentioned before, consider an *Aspergillus* in a culture as a contaminant and might well report it as such, if they reported at all, when it occurred in combination with a *Trichophyton*. However, the fact that superficial aspergillosis is not ordinarily produced experimentally supports the contention that lowered tissue resistance is necessary for its establishment. All our attempts to produce experimental infection of normal rabbit claws by inoculation with *A. nidulans* failed. Previous similar attempts with *A. flavus* in guinea pigs by Bereston and Keil<sup>6</sup> also failed. In addition their patient, whose infection was caused by *A. flavus* had a chronic severe bilateral pulmonary tuberculosis which definitely lowered tissue resistance. Therefore, aspergilli may be primary or secondary invaders of the nails and skin, however, in either case general or local diminished tissue resistance is a factor.

In contradiction to the aforementioned hypothesis, we may cite those few confirmed cases of aspergillosis in which no other fungus was recovered. In them a nutritional or metabolic dysfunction in the host might be considered as the cause of the lowered tissue resistance believed to be necessary for invasion by the aspergilli. Most likely a combination of these two theories explains the infection, either physiologic dysfunction or a lowered tissue resistance caused by a primary invasion by another fungus or by bacteria.

#### Results of Mycologic Examinations

| Sample,<br>Date | Site Taken         | Direct<br>Microscopic | Culture *            |   |              |              |
|-----------------|--------------------|-----------------------|----------------------|---|--------------|--------------|
|                 |                    |                       | Corn<br>Meal<br>Agar | Sabou-<br>raud's<br>Dex-<br>trose<br>Agar | Malt<br>Agar | Wort<br>Agar |
| 1<br>6/25       | Right foot, nail   | Positive              | A T                  | A T                                       | A T          | A T          |
| 2<br>6/25       | Left foot, nail    | Negative              | A T                  | A T                                       | A T          | A            |
| 3<br>7/2        | Right foot, nail   | Positive              | Neg                  | Neg                                       | Neg          | Neg          |
| 4<br>7/2        | Left foot, nail    | Positive              | Neg                  | Neg                                       | Neg          | Neg          |
| 5<br>7/2        | Left hand, nail    | Positive              | T                    | T   | T            | T            |
| 6<br>7/9        | Left foot, nail    | Positive              | T                    | T   | T            | T            |
| 7<br>7/9        | Left hand, nail    | Positive              | T                    | T   | T            | T            |
| 8<br>7/16       | Left foot, nail    | Positive              | A T                  | A T                                       | A T          | A T          |
| 9<br>7/16       | Right foot, nail   | Positive              | A T                  | A T                                       | A            | A            |
| 10<br>7/16      | Left hand, nail    | Positive              | A T                  | A T                                       | A T          | A T          |
| 11<br>7/28      | Left foot, nail †  | Negative              | Neg                  | Neg                                       | Neg          | Neg          |
| 12<br>7/28      | Right foot, nail † | Positive              | Neg                  | Neg                                       | Neg          | Neg          |
| 13<br>7/28      | Left hand, nail †  | Negative              | Neg                  | Neg                                       | Neg          | Neg          |
| 14<br>8/7       | Left foot, skin    | Positive              | A T                  | A T                                       | A T          | A T          |
| 15<br>8/23      | Left foot, skin    | Positive              | A T                  | A T                                       | A T          | A T          |
| 16<br>8/23      | Right foot, skin   | Positive              | A T                  | A T                                       | A T          | A T          |
| 17<br>8/23      | Left foot, nail    | Positive              | A T                  | A T                                       | A T          | A T          |
| 18<br>8/23      | Right foot, nail   | Positive              | A T                  | A T                                       | A T          | A T          |
| 19<br>8/23      | Left hand, nail    | Positive              | Neg                  | Neg                                       | Neg          | Neg          |

\* A, *Aspergillus nidulans*, T, *Trichophyton rubrum*

† Negative controls (samples of apparently normal nails)

neously in all the tubes inoculated precludes the idea that it was an incidental contaminant. The laboratory has handled large numbers of mycologic cultures and has never obtained more than an occasional contamination with aspergilli (W S W). Rockwood<sup>9</sup> in studying onychomycosis, pointed out in 1930 that in 1 case each of fifteen separate inoculations of mycologic mediums with material from one nail yielded an *Aspergillus*. She commented on the unlikely-

9 Rockwood, E M. A Study of Fungus-Infected Nails, Arch Dermat & Syph 22:395 (Sept) 1930

## SUMMARY AND CONCLUSIONS

Multiple fungous infections of the human nails and skin can occur, and a case of their occurrence was studied

*T. rubrum* was found in conjunction with *A. nidulans* in onychomycosis and dermatomycosis. The former may or may not have been the primary invader.

*A. nidulans* was identified for the first time as a cause of onychomycosis.

The aspergilli are apparently not always merely contaminants of mycologic cultures and although probably only mildly pathogenic for human beings they can invade human tissues under proper conditions.

It is hoped that this report will stimulate mycologists and dermatologists to study the aspergilli in their role as cutaneous pathogens.

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# UNDECYLENIC ACID IN THE TREATMENT OF DERMATOMYCOSIS

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The difficulties encountered in the evaluation of a fungicidal agent were well discussed recently by Goldman and his co-workers<sup>1</sup>. These authors pointed out that it is not possible to observe and control outpatients critically and frequently enough and that yet, if studies are carried out on hospital patients, the rest in bed creates artificial conditions "not similar to actual conditions under which the infection is usually acquired or aggravated or treated."

This study is based exclusively on outpatients. We felt that it was easier to surmount the shortcomings of control of such patients than to account for the beneficial effect of rest in bed, the extent of which is an unpredictable factor, making all conclusions uncertain.

In contrast to the studies made by Goldman and his associates, in this study only patients proved to have a fungous infection by scraping and/or culture were included. It is our firm conviction that the diagnosis of dermatomycosis of the foot must be made microscopically. The clinical differentiation of dyshidrosis from fungous infection is difficult, if not entirely impossible. Fungicidal agents which are well tolerated in the vesiculopustular form of dermatomycosis may often prove strong irritants in dyshidrosis. These agents, therefore, may be discredited as fungicides, and, vice versa, drugs without any fungicidal properties may be praised because they are found to have some beneficial effect on nonmycotic dyshidrotic eruptions.

A common error in the management of dermatomycosis is the application of the strongest possible fungicidal agent. The general practitioner often misjudges the irritability of the skin as well as the degree of disinfecting power required for treatment.

The requirements of a suitable fungicidal preparation are

From the Section of Dermatology, Department of Medicine, University of Chicago

1 Goldman, L., Henningsen, A. B., Ringelman, N. P., Fox, H. H., and Hesselbrock, J. Evaluation of a Fungicidal Agent for Fungous Disease of the Feet, *Arch. Dermat. & Syph.* **47**: 569-573 (April) 1943.

1 It should be able to kill the particular fungi.

2 It should be able to penetrate to the particular location of the fungi.

3 It should not irritate the skin in the particular phase of the disease in which it is applied.

A great number of drugs have been recommended for topical treatment of superficial fungous infection on the basis of their fungicidal action in vitro. Among them, iodine and sulfur head the list, whereas nonirritating mercurial preparations, such as ammoniated mercury, are of no value, and aniline dyes, such as gentian violet medicinal, are effective only in treatment of monilial infections.

Salicylic acid in itself has no great fungicidal power. Its action, however, is favorable because of its keratolytic effect. It causes a shedding of the horny layer, thus mechanically removing a great number of fungi. In addition, it facilitates the penetration of a fungicide with which it is combined. Ointment of benzoic and salicylic acid acts on this principle, but, in our experience, benzoic acid is a rather poor antimycotic agent in clinical use and moreover it is often irritating.

A new therapeutic principle was introduced in 1938 by Peck and Rosenfeld,<sup>2</sup> who found that organic fatty acids occurring in sweat have considerable fungicidal action without any irritating effect.<sup>3</sup> They found that the sodium salt of undecylenic acid has the strongest fungicidal action of all tested fatty acids and their salts.

2 Peck, S. M., and Rosenfeld, H. The Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on the Growth of Fungi, *J. Invest. Dermat.* **1**: 237-265 (Aug.) 1938.

3 A number of scattered references to the antimycotic action of fatty acids can also be found in the literature of earlier decades. Clark, J. F. On the Toxic Effect of Deleterious Agents on the Germination and Development of Certain Filamentous Fungi, *Botan. Gaz.* **28**: 289-327 and 378-402, 1899; Electrolytic Dissociation and Toxic Effect, *J. Physiol. Chem.* **3**: 263-316, 1899; Kissel, A. Recherches sur l'action de divers acides and sels acides sur le developement de l'*Aspergillus niger*, *Ann. Inst. Pasteur* **27**: 391-420, 1913.

Undecylenic acid, an unsaturated fatty acid with 11 carbon atoms, has the formula  $\text{CH}_2\text{CH}(\text{CH}_2)_8\text{COOH}$ . Its melting point is  $24.5^\circ\text{C}$ , and its boiling point  $155^\circ\text{C}$  (at a pressure of 10 mm of mercury).

Rigler and Greathouse<sup>4</sup> found undecylenic acid itself highly fungicidal. They stated that in a homologous series of fatty acids the activity was proportionate to the length of the aliphatic chain up to 11 carbon atoms. It also has been claimed<sup>5</sup> that unsaturation increases the fungistatic effectiveness of a fatty acid. Thus, undecylenic acid and its salts seemed to be the most effective compounds in this series.

During the past two years we tested a preparation consisting of zinc undecylenate (20 per cent) and undecylenic acid (5 per cent) in a

of 102 healthy Army Air Corps students examined for dermatomycosis of the feet. The 50 members of the second group with known fungous infections could be observed for a period of from one to four weeks only, whereas for the clinical group we attempted to establish a longer observation period. Because of this difference the two groups will be discussed separately.

All patients selected for treatment were given a jar of undecylenate ointment and were advised to rub it thoroughly into the affected areas once daily. For those with dermatomycosis pedis all interspaces were treated without regard to clinical appearance.

The clinical form of the dermatomycosis, the findings on culture and the results of therapy in the outpatient group are summarized in table 1.

DERMATOMYCOSIS PEDIS

In the group with dermatomycosis pedis were included patients with vesicular, vesiculopustular,

TABLE 1—Clinical Form of Dermatomycosis, Cultural Observations and Results of Therapy in the Outpatient Group

| Diagnosis                        | Cultural Results          | Results of Therapy |                        |          |         |
|----------------------------------|---------------------------|--------------------|------------------------|----------|---------|
|                                  |                           | Number of Cases    | Complete Clinical Cure | Improved | Failure |
| Dermatomycosis of feet           | T. gypsum                 | 21                 | 18                     | 1*       | 2       |
|                                  | T. purpureum              | 2                  | 1                      |          | 1       |
|                                  | E. inguinale              | 3                  | 3                      |          |         |
|                                  | M. albicans               | 9                  | 9                      |          |         |
|                                  | Microscopic evidence only | 28                 | 26                     | 1*       | 1†      |
|                                  | Total                     | 63                 | 57                     | 2        | 4       |
| tinea circinata (tinea corporis) | T. gypsum                 | 2                  | 1                      |          | 1       |
|                                  | M. audouinii              | 1                  | 3                      |          |         |
|                                  | Microscopic evidence only | 4                  |                        |          | 1       |
|                                  | Total                     | 7                  | 4                      | 0        | 3       |
| tinea cruris and axillaris       | M. albicans               | 1                  | 1                      |          |         |
|                                  | Microscopic evidence only | 5                  | 5                      |          |         |
|                                  | Total                     | 6                  | 6                      | 0        | 0       |
| Onychomycosis                    | T. gypsum                 | 1                  |                        |          | 1       |
|                                  | M. albicans               | 4                  |                        | 3        | 1       |
|                                  | Microscopic evidence only | 4                  |                        | 3        | 1       |
|                                  | Total                     | 9                  | 0                      | 6        | 3       |
| Tinea capitis                    | M. audouinii              | 11                 | 3                      | 2        | 6       |

\* Observed less than four weeks.  
† In this case Fusarium was found on culture.

vanishing emulsion base ( $p_H$  6.5).<sup>6</sup> The following is a report on our results with this preparation, which will be referred to in the paper as undecylenate ointment.

CLINICAL MATERIAL

The material studied comprises two groups of persons, the first consisting of 100 regular outpatients of the clinic with known fungous infections and the second

4 Rigler, N. E., and Greathouse, G. A. The Chemistry of Resistance of Plants to Phymatotrichum Root Rot. VI. Fungicidal Properties of Fatty Acids, Am. J. Botany 27:701-704 (Oct.) 1940.

5 Hoffman, C., Schweitzer, T. R., and Dalby, G. Fungistatic Properties of the Fatty Acids and Possible Biochemical Significance, Food Research 4:539-545 (Nov.) 1939.

6 The material for this study was supplied by the Research Department of Wallace and Tiernan Products, Inc., Belleville, N. J.

erosive, dry scaling, macerated and fissuring and hyperkeratotic forms. The therapeutic results were the same for all these forms except that the improvement was slower in the hyperkeratotic form. Erosions remaining after rupture of vesicles and bullae and fissures were not regarded as contraindications for treatment with the undecylenate ointment, which was well tolerated in such cases even if the erosions and fissures were rather extensive. However, no fungicidal treatment was initiated in cases of dermatomycosis with extended diffuse, oozing dermatitis with or without secondary infection, and such cases are not included in our study.

The effect of undecylenate ointment was conspicuously rapid in producing symptomatic relief as well as reducing the signs of inflammation for 59 of 63 outpatients. Most patients stated

that itching stopped overnight immediately after the first application. The spread of the process was also completely checked, and fungi could not further be demonstrated microscopically or culturally after treatment had been initiated. The time necessary for achieving complete clinical cure is shown in table 2. The table demonstrates that in the great majority of the cases (86 per cent) complete clinical cure was accomplished within four weeks.

TABLE 2—*Distribution of the Time Periods Required for the Complete Clinical Cure of Dermatomycosis Pedis*

| No. of Weeks | No. of Cases | Per Cent |
|--------------|--------------|----------|
| 1            | 8            | 14.0     |
| 2            | 19           | 33.3     |
| 3            | 13           | 22.8     |
| 4            | 9            | 15.8     |
| 5            | 3            | 5.2      |
| 6 to 8       | 2            | 3.5      |
| 9 to 12      | 2            | 3.5      |
| 26           | 1*           | 1.7      |

\* Hyperkeratotic form.

Attempts were made to compare these favorable results with results obtained by older routine methods. Patients were asked to apply the investigational ointment on one foot and an ointment of 2 per cent salicylic acid and 3 per cent sulfur incorporated into the same ointment base on the other foot simultaneously. In a few cases comparisons were made with sulfur-salicylic acid ointments of higher concentration and with Castellani's paint.

There were 18 patients concerning whose infections a definite opinion could be formed from such comparative experiments. For 10, undecylenate ointment proved to be superior to the older preparations, for 7, equal, and for 1, inferior. Superiority of undecylenate ointment manifested itself in more rapid effect and in non-irritation. In addition to these results of simultaneous parallel experiments observed by us, the majority of our patients stated that undecylenate ointment was definitely superior to any other preparation they had used previously.

After complete clinical cure was obtained, one group of patients was asked to continue treatment for a longer period and another group was put on observation without treatment. In the first group, 20 patients were followed during an observation period of from one to twenty months (table 3). All patients who treated themselves continuously remained completely free of signs and symptoms. Repeated microscopic and cultural examinations yielded negative results. In the second group, 12 patients could be satisfactorily checked. Four of them

had no relapses during an observation period of two, seven, ten and eleven months, respectively, after cessation of treatment. The patients had relapses three, five and eight months, respectively, after clinical cure was achieved. Five patients had numerous relapses during observation periods longer than one year. All these patients stated that clinical cure and relapses was easily accomplished on resumption of treatment but that new lesions appeared soon after cessation of treatment.

Although the number of patients in this group who could be followed long enough, unfortunately, is small, the following conclusions can safely be made:

1. Relapses can regularly be avoided by continuous treatment.

2. Complete clinical cure achieved by the fungicidal preparation does not protect against relapses after treatment has been discontinued.

Two thirds of our patients who discontinued treatment had recurrences some time during the observation period. Of course, it could not be determined whether these recurrences were relapses from quiescent foci or newly acquired infections. It certainly was a new infection in two of our patients from whose lesions different species of pathogenic fungi were grown on culture during the first eruption and during the "relapse." In general, it is difficult to decide whether a new eruption represents relapse or new infection, because the source of infection,

TABLE 3—*Duration of Follow-up Period in Which No Relapses Occurred After Clinical Cure*

| Months | Number of Cases |
|--------|-----------------|
| 1      | 2               |
| 2      | 3               |
| 3      | 1               |
| 4      | 5               |
| 6      | 1               |
| 7      | 1               |
| 8      | 1               |
| 9      | 4               |
| 11     | 1               |
| 20     | 1               |

though not ubiquitous, is extremely widespread in this country.

In 4 of the 63 patients the fungous infection could not be cleared up with the investigational preparation.

The first patient had an infection with *Trichophyton purpureum* involving the interspaces of toes and nails. There was no clinical improvement of the skin after one month of treatment with undecylenate ointment. During the following two weeks no improvement was achieved with an ointment of 5 per cent sulfur and 2 per cent salicylic acid. Subsequently, an ointment

containing 10 per cent sulfur and 5 per cent salicylic acid brought about clinical cure of the skin

The second patient presented a vesiculopustular eruption of the toes, from which *Trichophyton gypseum* was grown on culture, and eczematoid lesions of the ankles, which did not contain fungi and which were diagnosed as dermatophytids. Contrary to advice, this patient applied the investigational ointment not only to the toes but also to the "id" lesions. The treatment resulted in a violent irritation of all lesions and in the outbreak of a new vesicular dermatophytid on the arms. This was the only patient in whom irritation and mobilization were caused by undecylenate ointment.

Scrapings from scaling lesions of the toes of the third patient showed questionable spores, and the culture yielded *Fusarium*, this fungus is generally regarded as nonpathogenic. The investigational preparation was found clinically ineffective after two weeks, and subsequently the application of an ointment of 10 per cent sulfur and 3 per cent salicylic acid resulted in complete clinical cure within three weeks.

*T. gypseum* was grown on culture of materials from the lesions of the toes of the fourth patient. Application of undecylenate ointment did not check the spread of the process. Similarly the application of sulfur-salicylic acid ointment failed. The patient notified us that the dermatomycosis was finally cleared up by some proprietary remedy.

The failure in treatment of the first patient might have been interpreted as an indication that undecylenate ointment is not effective in infections with *T. purpureum*, which, in general, are relatively resistant to any kind of treatment. However, in our only other case of such infection, the response was satisfactory. Also, in vitro experiments indicated that undecylenic acid and its salts are highly effective against *T. purpureum*. Therefore, the effect of undecylenate ointment on this particular fungus needs further investigation.

The case of the second patient illustrates that when there is a high degree of allergy, particularly in the presence of "ids," the greatest caution is required in application of any fungicidal agent, including undecylenate ointment.

It is impossible to interpret satisfactorily the failure in treatment of our third patient. *Fusarium*, like a mold, possibly suppressed the development of a therapeutically resistant pathogenic species on the culture medium.

The case of the fourth patient represents an outright failure of the preparation in treatment of common "athlete's foot" infection. Of course, we cannot be sure that the patient strictly followed the instructions given him.

In the group of Army Air Corps students, 102 persons either gave a positive history of fungous infections or presented clinically suggestive signs of dermatomycosis pedis. From 50 of the 102 patients positive microscopic and/or

cultural evidence of the fungi was obtained.<sup>7</sup> In 15 patients the fungi were demonstrated both microscopically and culturally, in 25 they were seen microscopically but not culturally, and in 10 they were seen culturally but not microscopically. These statistics indicate that both microscopic and cultural methods should be used in order to obtain maximum aid from the laboratory.

In the 25 instances in which fungi were grown on culture they were identified as follows: *T. gypseum* 8, *Monilia albicans* 10, *Epidermophyton inguinale* 5, *Sporotrichum* (nonpathogenic) 1 and *Cephalosporium* (nonpathogenic) 1. These cultural observations are combined with those of the outpatient group in table 4.

TABLE 4—*Cultural Observations in Dermatomycosis Pedis*

| Organism              | Number of Cases |
|-----------------------|-----------------|
| <i>T. gypseum</i>     | 29              |
| <i>T. purpureum</i>   | 2               |
| <i>E. inguinale</i>   | 8               |
| <i>M. albicans</i>    | 19              |
| <i>Sporotrichum</i>   | 1               |
| <i>Cephalosporium</i> | 1               |
| <i>Fusarium</i>       | 2               |
| Total                 | 62              |

The 50 members of the group with positive evidence of fungi were treated for from one to four weeks. Twenty-nine patients could be re-examined within the four weeks of treatment. Complete clinical cure was achieved for 14 patients and clinical cure with questionable remnants of scaling for 12 patients, and 3 patients still had an active infection. No difference in the response to the fungicidal agent according to cultural result was noted.

The opinion of the members of the group as to the efficacy of the undecylenate preparation as compared with that of previously used preparations was as follows: undecylenate ointment definitely superior, 15, equal 3, inferior, 0, and no basis for comparison, 11. Previous types of remedies included ointment of benzoic and salicylic acid, Castellani's paint, mercurial preparations and various proprietary remedies.

In addition to the efficiency of the undecylenate preparation, the vanishing emulsion base was regarded by most of the soldiers as the most pleasant and convenient method of application.

<sup>7</sup> At the time of examination many students were using some kind of routine treatment (ointment of benzoic and salicylic acid, powders and so forth), and this treatment may account for the fact that the organism could be recovered in only about 50 per cent of the cases.



## TINEA CIRCINATA (TINEA CORPORIS)

" This group includes 9 patients with clinically typical and microscopically proved ringworm of the glabrous, nonintertriginous skin. On culture of materials from the lesions of 3 patients *Microsporon audouinii* and of 2 *T. gypsum* were grown. In culture of materials from the lesions of the remaining 4, no pathogenic fungi grew on Sabouraud's medium. For the patients infected with *M. audouinii*, complete clinical cure was achieved with the undecylenate ointment within a few days, and no relapse was observed within two months.

The infection with *T. gypsum* of the glabrous skin was not so well influenced. For 1 patient with an erythematosquamous ringworm lesion, treatment had to be continued for two months before complete clinical cure was obtained. Treatment of the other patient, with a vesiculopustular ringworm lesion, was a complete failure, the spread of the vesiculopustular border was not checked by undecylenate ointment, and irritation was present. After ten days the treatment had to be changed to application of a 2 per cent solution of iodine in benzene and an ointment of 3 per cent sulfur and 2 per cent salicylic acid. This treatment resulted in complete clinical cure after five days.

The great difference in efficiency of undecylenate ointment in treatment of *T. gypsum* infections of intertriginous and nonintertriginous regions is not well understood, and our material has not been sufficient to allow us to draw any conclusions.

In treatment of the 4 patients whose lesions showed no cultural growth of pathogenic fungi, undecylenate ointment definitely failed. Subsequently clinical cure was achieved in a few days by combined application of a 2 per cent solution of iodine in benzene and ointments containing from 3 to 10 per cent sulfur and from 2 to 3 per cent salicylic acid. It is difficult to interpret these cases, because the causative agent of the infections is unknown. In culture of materials from 2 patients bacteria grew in the culture tubes, from 1 mold and from 1 *Fusarium*. Some pathogenic species might have been suppressed by these saprophytes, because in direct microscopic examination of scrapings hyphae and spores were seen such as are found in scrapings in which pathogenic fungi are present. However, the pathogenic fungus probably was not *T. gypsum*, because this species is not easily suppressed by secondary infection.

## TINEA CRURIS AND AXILLARIS

Regardless of the nature of the causative agent (table 1), for these 6 patients with intertriginous

localization of the infection undecylenate ointment effected rapid clinical cure in one to four weeks. No relapse was observed in this group. In 2 patients the mycotic process had spread from the flexural surfaces to the nonintertriginous skin and had involved rather extensive areas. Nevertheless, the cure was surprisingly rapid in these localizations, too.

## ONYCHOMYCOSIS

All 9 patients with fungous infection of the nails were advised to file down and trim the nails before applying the ointment. Grinding with a dental drill was done in the clinic.

No complete clinical cure was achieved by application of undecylenate ointment, but definite improvement was noted in 6 patients (table 1). In treatment of 3 of these 6 patients, undecylenate ointment was superior to gentian violet medicinal, an iodine solution in benzene, strong sulfur-salicylic acid ointments and 20 per cent chrysarobin ointment used previously. One patient who had been treated continuously for one and half years with fungicides without improvement was particularly benefited by the new drug.

In treatment of 3 patients undecylenate ointment was ineffective in spite of continuation of treatment for several months. Subsequently, 1 patient was improved slightly by chrysarobin ointments, the 2 others were not benefited by sulfur-salicylic acid ointments and by a 2 per cent solution of iodine in benzene.

## TINEA CAPITIS

Eleven patients with tinea capitis, all infections caused by *M. audouinii*, were treated. It has been a generally accepted view that infection with the microsporon of human origin, as contrasted with infection with *M. lanosum*, of animal origin, cannot be eradicated by fungicidal preparations alone but that temporary epilation of the scalp by roentgen rays has to precede fungicidal treatment. In our experience, this view has been found to be true in general, but there have been patients who could be completely cured by application of strong sulfur ointments without preceding epilation. Livingood and Pillsbury<sup>8</sup> stated that in their series of 105 cases of *M. audouinii* infection of the scalp 27 per cent of the patients were cured without roentgen epilation.

Among our 11 patients, all of whom were frequently checked by examination under fluores-

<sup>8</sup> Livingood, C. S., and Pillsbury, D. M. Ringworm of the Scalp, *J. Invest. Dermat.* 4:43-57 (Feb) 1941.

cent light and microscopically, 3 were completely cured by undecylenate ointment. Eight were not cured. To make comparison, subsequent to the unsuccessful treatment with undecylenate ointment the 8 patients were given strong sulfur-salicylic acid ointments. The result was no better, so roentgen epilation was indicated.

#### ADDITIONAL OBSERVATIONS

In treatment of 1 patient with tinea versicolor, 1 patient with erythrasma and 1 patient with granulating eroded cutaneous lesions of coccidioidal granuloma, undecylenate ointment was ineffective.

Early in this study, undecylenic acid and its zinc salt were also tried in a dusting powder base (zinc undecylenate 20 per cent, undecylenic acid 2 per cent, in purified talc U S P) in treatment of dermatomycosis pedis. The results were similar to those obtained with the ointment when the powder was massaged vigorously into the skin. This procedure, however, was obviously more difficult for the patient to carry out than was massage with ointment. Therefore, the results were variable, and the method was far more unreliable than that in which the ointment was used. In a few cases, undecylenate powder was given to the patients for prophylactic purposes, and no relapses were reported during the period in which it was used.

#### SUMMARY AND CONCLUSIONS

1 A new fungicidal preparation containing 20 per cent zinc undecylenate and 5 per cent undecylenic acid in vanishing emulsion base ( $p_H$  6.5) was tested clinically on a total of 150 patients with dermatomycosis presenting positive microscopic and/or cultural evidence of fungi.

The group of patients with dermatomycosis of the feet included 113 patients. Among 62 fungi grown on culture in this group, 46.7 per cent were *T. gypsum*, 3.2 per cent were *T. purpureum*, 12.9 per cent were *E. inguinale*, 30.6 per cent were *Monilia*, and 6.2 per cent were fungi usually considered to be nonpathogenic.

The other clinical forms of dermatomycosis were represented by substantially smaller groups.

2 Complete clinical cure could be achieved with the undecylenate preparation within four weeks for the great majority of patients (86 per cent) with dermatomycosis pedis, regard-

less of the species of causative fungi. Relapses did not occur if treatment was continued.

This result does not indicate that the new preparation is far superior in fungicidal action to older standard preparations, particularly to sulfur-salicylic acid ointments. In fact, comparative experiments have shown that the new preparation is only slightly superior to sulfur-salicylic acid preparations. However, the undecylenate ointment is less irritating than any other preparation of similar fungicidal strength. We never would risk initiating treatment with tincture of iodine or sulfur-salicylic acid ointments of the required strength for patients with extended vesiculation, erosions, rhagades and edema of the feet, whereas this can be done with the undecylenate ointment without the slightest danger of irritation. The virtue of the new preparation is that it is nonirritating and still strongly fungicidal.

3 In treatment of tinea cruris and tinea axillaris, also, complete clinical cure was accomplished easily with the undecylenate preparation, regardless of the causative agent. In this group complete absence of any irritating action was noted as particularly important because of great irritability of large flexural surfaces.

4 Against tinea circinata the results so far are not entirely satisfactory. We are unable to explain the less favorable effect of undecylenate ointment on nonintertriginous skin as compared with the skin of intertriginous regions.

5 Infection of the glabrous skin with *M. audouinii* in adults and children responded extremely well. In addition, 3 out of 11 patients with tinea capitis caused by *M. audouinii* were cured by the undecylenate ointment, so that roentgen epilation was not necessary.

6 In treatment of onychomycosis our results were not encouraging.<sup>9</sup>

Dr. George M. Lewis, of Cornell University, and Dr. C. W. Emmons, of the United States Public Health Service, identified several species of nonpathogenic fungi.

J. K. Anderson and W. E. Parker, of the Athletic Department of the University of Chicago, arranged for us to examine the Army Air Corps trainees.

Dr. Zachary Felsher and Miss Dorothy Shaw gave technical assistance.

9 Since this paper was submitted, the fungicidal action of undecylenic acid has been favorably reported on by A. B. Hillegas and E. Camp (*J. Invest. Dermat.* 6:217-226 [June] 1945) and by M. B. Sulzberger, H. C. Shaw and A. Kanof (*U. S. Nav. M. Bull.* 45:237-248 [Aug.] 1945).

## POLYCYTHEMIA WITH AN UNUSUAL ERUPTION

ALBERT STRICKLER, M D

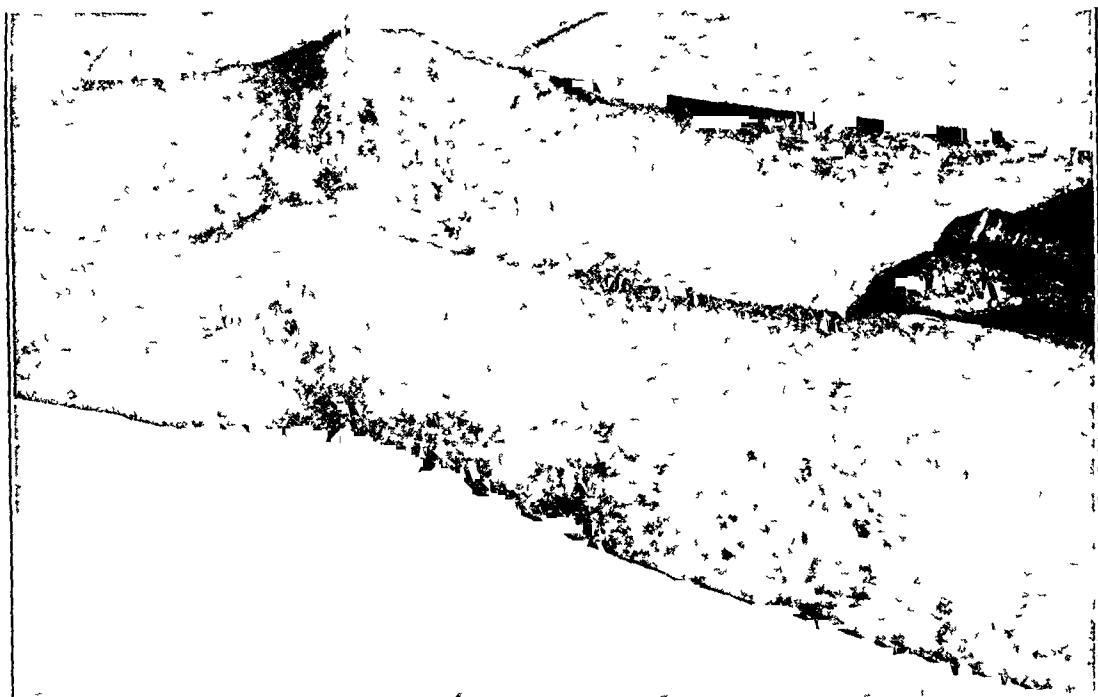
PHILADELPHIA

Two cutaneous manifestations have been described in association with polycythemia a purplish redness of the gums, due to a high concentration of hemoglobin, and a papular urticarial eruption with a surmounting vesicle or pustule occurring in crops, decidedly itchy and with bloody crusts. This eruption has unfortunately been termed *acne urticata polycythæmica* (Kaposi). Up to the present about 12 cases have been reported.

Klauder<sup>1</sup> reported an instance of such an eruption in a patient who presumably suffered

spleen were enlarged. The blood had a high uric acid content. The blood count showed erythrocytes, 5,000,000 to 5,800,000, hemoglobin content, 110 per cent, and leukocytes, 20,000. In the differential count, there were 90 per cent polymorphonuclear leukocytes, 4 per cent lymphocytes, 2 per cent eosinophils and 4 per cent myelocytes.

Criteria justifying a diagnosis of polycythemia are a change in appearance, enlargement of the spleen and excess of red corpuscles in the blood. The superficial blood vessels, capillaries and



Polycythemia accompanied with a dermatitis-herpetiformis-like eruption

from polycythemia although there was some doubt as to whether the disease might have been leukemia. The patient was a white woman, aged 58, who suffered from an itchy papular eruption which persisted and which occurred in crops. The primary lesion was an urticarial papule with a vesicle or pustule on top. The patient had hypertension, and the liver and

veins seem full, and the skin is always congested. The engorgement of the face may be extreme and may extend to the conjunctivas. The spleen is usually enlarged, hard and painless. The polycythemia is variable, the red blood cell count ranging from 7,000,000 to 12,000,000 or even 13,000,000 per cubic millimeter. The hemoglobin level ranges up to 150 per cent, but the color index rarely reaches 1. A moderate

From the dermatologic clinic, the Skin and Cancer Hospital, Albert Strickler, M D, Director

<sup>1</sup> Klauder, J V. *Acne Urticata Polycythæmica*, Arch Dermat & Syph 38 145 (July) 1938

<sup>2</sup> Osler, W. *Principles and Practice of Medicine*, edited by H A Christian, ed 14, New York, D Appleton-Century Company, Inc, 1942, p 969

elevation of leukocytes is the rule. The common symptoms are headache, dizziness, paresthesia, paresis and paralysis. In the differential diagnosis of polycythemia one must consider congenital heart disease, emphysema and poisoning from coal tar products.

#### REPORT OF A CASE

C. D., a white man, aged 54, reported at the Skin and Cancer Hospital, complaining of an eruption of one year's duration. The eruption started at the navel, extended to the axillae and groins and finally covered the entire body.

On dermatologic examination the face presented congested patches, which persisted, the nose was enlarged and presented dilated capillaries. The conjunctivae were suffused and the eyelids swollen. Especially in the axillae and in the groins there were margined patches consisting of small vesicles, pinhead sized to pea sized, situated on an erythematous base. They were closely aggregated and caused no decided subjective discomfort. The vesicles had a pearly appearance and closely simulated dermatitis herpetiformis, some were pustular. On the extremities in various areas there were groups of vesicles without definite arrangement. The mucous membranes were not involved.

*Physical Examination*—The following abnormalities were observed: slight emphysema of the lungs with no rales, slight enlargement of the heart, with the heart sounds good and regular, a decided enlargement of the liver and the spleen, both of which were firm and painless, and generalized adenopathy.

*Laboratory Studies*—The blood counts were as follows: The hemoglobin level varied between 119 and 131 per cent, the erythrocytes remained about 6,400,000 per cubic millimeter. The differential count showed 84 per cent polymorphonuclear leukocytes and 13 to 16 per cent lymphocytes. The number of blood platelets was 220,000 per cubic millimeter. The sedimentation rate was 0.25 mm after sixty minutes. The blood

chemistry was as follows: sugar, 100 mp., urea nitrogen, 23 mg., and uric acid, 5 mg. The Wassermann and Kahn tests elicited negative reactions. A culture of the lesions yielded *Staphylococcus albus*. The urine contained a trace of albumin and hyaline and granular casts.

*Histologic Examination*—One of the lesions was excised for histologic study and a section of skin was stained with hematoxylin and eosin. The report is as follows:

*Epidermis*—The stratum corneum is present in most of the lesion, except for one area in which there is evidence of ulceration, and in this area there is parakeratosis as well as a polymorphonuclear leukocytic infiltrate. In another area in the epidermis there is a focus of infiltration by inflammatory cells which have not broken through to the surface. The rete is acanthotic, and its cells show intercellular and intracellular edema. The epidermis-dermis junction is normal.

*Cutis*—The blood vessels are greatly dilated, and many contain red blood cells and some fibrin. Collections of red cells are seen here and there outside the blood vessels. The infiltrate, which is diffuse and high in the cutis, consists of lymphocytes and connective tissue cells, epithelioid cells, mononuclear and polymorphonuclear leukocytes, eosinophils and plasma cells. The eosinophils are numerous, and many of them are eosinophilic plasma cells. In the midcutis a similar infiltrate is seen largely about the blood vessels. The lumens of the blood vessels do not present any decided abnormality. The sweat apparatus is apparently normal.

*Treatment*—With high voltage roentgen irradiation and frequent bleedings the eruption has almost entirely disappeared, except for the lesions in the groins, which are also showing great improvement.

#### SUMMARY

A vesicular eruption simulating dermatitis herpetiformis occurred in a patient suffering from polycythemia.

327 South Sixteenth Street

## CREEPING ERUPTION

### RESULTS OF TREATMENT WITH FUADIN

CAPTAIN FRANK A DOLCE AND MAJOR JOHN E FRANKLIN

MEDICAL CORPS, ARMY OF THE UNITED STATES

The treatment of creeping eruption by freezing the larvae in situ with either ethyl chloride spray or solid carbon dioxide is well known. Although this method is effective, it is tedious in cases of widespread involvement and is not efficient in controlling the intense itching until all the larvae are killed. In addition, we do not use this form of treatment on severely excoriated and secondarily infected areas. A method of treatment which would quickly control the itching and could be promptly used in all cases would be a distinct advancement in the therapy for this disease.

The recent reports in the literature of the successful use of fuadin in the treatment of creeping eruption by Smith,<sup>1</sup> Wilson<sup>2</sup> and Rubin<sup>3</sup> suggested that this is the method of choice. We therefore treated a group of 14 patients with creeping eruption with fuadin to determine the efficacy of this method. We wish to report our results with this group and to review the recent literature on the subject.

Smith<sup>1</sup> reported the successful treatment of creeping eruption with fuadin in a boy 2½ years old. Treatment was stopped after eight injections. The dose used was 2 cc. Wilson<sup>2</sup> reported the successful treatment of creeping eruption with fuadin in a series of 8 cases. In 5 cases the patients were cured after one injection, and in 2, the patients were cured after two injections. Rubin<sup>3</sup> reported the case of a soldier with thirty-two larvae who was treated with twelve injections of fuadin. At the end of this course of treatment only one larva was present, which was destroyed with ethyl chloride spray. Blank,<sup>4</sup> on the other hand, reported a case in which treatment was unsuccessful after ten injections of fuadin.

We have used fuadin in treatment of a group of 14 patients with creeping eruption. This group consisted of military personnel or their dependents. There were 12 adults and 2 children. All gave a history of either spending considerable time on the sand along the beaches of Florida or walking barefooted on damp soil. The diagnosis was made from the characteristic clinical picture of an advancing tortuous erythematous burrow with an erythematous papule at the advancing end and associated with severe itching. No attempt was made to identify the larva. It was assumed that the larva was that of the *Ancylostoma braziliense*. The number of larvae present varied from one in 2 patients to well over one hundred in 2 patients. Three patients had three larvae, 5 patients had ten larvae, 1 patient had thirty larvae, and 1 patient had thirty-six larvae.

The plan of treatment was to give the patient 2 cc. of fuadin the first day, and if there were no symptoms of intolerance the dose was increased to 5 cc. the next day and was continued daily for five days. No one received more than 5 cc. of fuadin in one dose. The children received one half of this dose. If more than five injections of fuadin were decided on, it was then given every other day. The injections were given deep into the gluteal muscle. The urine was examined prior to each injection. The patients were questioned in regard to relief of itching at each visit. The involved area or areas were examined each time. The number of injections given to each patient and the results are shown in the accompanying table.

*Results of Treatment*

| Number of Injections | Number of Patients | Results   |
|----------------------|--------------------|-----------|
| 13                   | 1                  | No effect |
| 10                   | 1                  | No effect |
| 6                    | 2                  | No effect |
| 5                    | 7                  | No effect |
| 8                    | 1                  | Improved  |
| 5                    | 2                  | Cured     |

Two patients were completely cured with fuadin, and 1 was improved. This patient had had thirty-six larvae prior to treatment. At the

1 Smith, D. C. The Treatment of Creeping Eruption with Sodium Antimony Biscatechol (Fuadin), J A M A 123 694 (Nov 13) 1943

2 Wilson, J. F. The Treatment of Creeping Eruption with Fuadin, J Florida M A 30 425 (April) 1944

3 Rubin, S. S. Creeping Eruption, J A M A 124 668 (March 4) 1944

4 Blank, H. Use of Fuadin in Creeping Eruption, J A M A 123 989 (Dec 11) 1943

completion of the course of treatment only six advancing pruritic burrows remained. Treatment with fuadin was stopped after eight injections because the patient complained bitterly of itching and said that it interfered with sleep. Two patients whom we previously had classified as having been successfully treated with five injections of fuadin returned several weeks later with recurrence of itching and reactivation of the larvae at the original sites. There was no reduction in the number of larvae present. In these 2 cases we considered that treatment had failed and not that the sites had been reinfested. We were justified in this opinion because it would be highly improbable for a reinfestation to occur at the same sites and with the same number of larvae and because at the completion of the course of treatment a number of mildly pruritic papules corresponding to the original number of larvae were present. These papules were re-

garded at that time as highly suggestive of containing resting larvae. All the patients for whom treatment had been unsuccessful were treated with either ethyl chloride spray or a local application of solid carbon dioxide. In the 2 patients cured with fuadin, the relief of itching was immediate. This relief occurred in both patients after the second injection.

It is our opinion from this rather small group of patients that the use of fuadin as employed by us in the treatment of creeping eruption is inferior to the older methods of freezing the larvae. We have found this method effective in too few cases to continue its further use.

#### SUMMARY

The results of treatment with fuadin of 14 patients with creeping eruption were unsatisfactory in all but 2 instances.

## XERODERMA PIGMENTOSUM

ADDITIONAL NOTES ON THE SIX CASES OF DR MAYRAND AND DR GAUMOND

MADGE THURLOW MACKLIN, M D

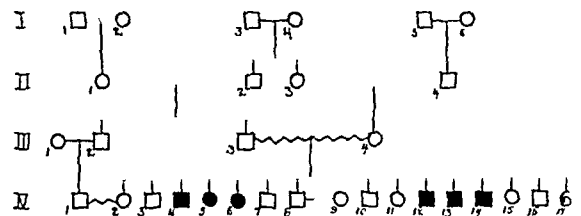
LONDON, ONTARIO, CANADA

After the publication of the article on xeroderma pigmentosum which appeared in the March 1944 issue of the ARCHIVES,<sup>1</sup> Dr Gaumond, of the city of Quebec, called my attention to a family on which he had first reported in 1934<sup>2</sup> and again, with Dr Mayrand, in 1936<sup>3</sup> and in which there were 6 children affected with this disease. The journals in which these accounts appeared, together with many others, were not available, and hence this family was omitted from the analysis in that paper. Dr Gaumond sent me a copy of the report, the parents of the family of 14 children, 6 of whom had xeroderma pigmentosum, were first cousins. The sex of some of the normal offspring was not given. I asked Dr Gaumond to furnish me with the data (1) as to the sex of all the children in the family and (2), if possible, as to the manner in which the parents were related. He was able to secure the first item of information, but he was not able to obtain the second because the family did not live in Quebec and apparently did not understand his question by correspondence.

I appealed to Mr Georges Lachapelle, a French Canadian student in the University of Western Ontario Medical School, for assistance asking him to obtain the information for me, if possible by a direct visit to the family or to the parish priest of the locality. His sister, Dr Pauline Lachapelle, of Mont Laurier, Quebec, made a round trip of 80 miles (128 kilometers) to the village in which the family lived, interviewed the mother and obtained for me the desired information. Because I have encountered no other family in which as many as 6 children were affected and in which the manner of the relationship of the parents was given, I am pub-

lishing, with Dr Gaumond's permission, the additional information received from him as to the sex of the normal offspring and from Dr Lachapelle as to the manner in which they were related, in order that this information may be made available for those who wish to study sex distribution in such families in the future.

It will be noted that the father's father and the mother's mother were brother and sister. Thus the defective gene, if xeroderma pigmentosum is partially sex linked, came to the father, Th Bou, through his father Jo Bou. One would expect only sons to be affected if there were no crossing



Generation I 1 Lo Pru 2 Name unknown 3 Fab Bou 4 Hel ? Maiden name unknown 5 Mar Kir 6 Fra Gag

Generation II 1 Ad Pru 2 Jo Bou 3 Lez Bou 4 Mar Kir

Generation III 1 Del Gir 2 Ovide Bou 3 Th Bou, died at 51 of pneumonia 4 Phi Kir

Generation IV 1 Ovila Bou married in 1938 to his first cousin, 2 Ber Bou, who was born in 1907 3 Luc Bou born 1908 4 Leo, affected, born 1909 5 Luc, affected, born 1910 6 Leo, affected, born 1911 7 Arm born 1913 8 Rom born 1916 Married in 1940 to 9, who is not related to him 10 Pa born 1920 11 Ros born 1921 12 Phi, affected, born 1923 13 Ant, affected, born 1923, not a twin to 12 14 Ev, affected, born 1926 15 Jea, born 1928 16 Died, aged 1 day 17 Six miscarriages occurring at the period of three or four months and occurring before the birth of 16

White symbols represent normal persons, black symbols represent persons affected with xeroderma pigmentosum. Squares represent males and circles females. The saw-toothed lines joining males and females indicate consanguineous marriages. III, 3 and III, 4 were first cousins. IV, 1 and IV, 2 are doubly related, being first cousins because they are the offspring of brothers and being second cousins because they are the offspring of first cousins, III, 2 and III, 4. As yet there are no offspring of these two marriages in the fourth generation.

Parts of the names of these persons have been included so that should the disease reappear in subsequent generations the identity of this pedigree with that newly reported could be determined, but not enough has been given to reveal the identity of the family otherwise.

From the University of Western Ontario Medical School

1 Macklin, M T. Xeroderma Pigmentosum. Report of a Case and Consideration of Incomplete Sex Linkage in Inheritance of the Disease, Arch Dermat & Syph 49 157 (March) 1944

2 Gaumond, E. Xeroderma Pigmentosum, Bull Soc med d hôp Universitaires de Quebec, February 1934, p 79

3 Mayrand, R, and Gaumond, E. Xeroderma Pigmentosum. Six cas. Quatre freres et deux soeurs d'une meme famille, Bull Assoc d med de lang franç de l'Amerique du Nord, January 1936



over in the sex chromosomes or more sons than daughters to be affected if crossing over had occurred. The latter was the case, 4 sons being affected and only 2 daughters. One would expect that half of the sons would be affected, and, again, this is true. There were 8 sons who lived, and, of these, 4 became affected. In the families reported on in the earlier paper,<sup>1</sup> when the defect presumably came through the Y chromosome, as evidenced by the fact that only males were affected, or when it was known that it did come through the Y chromosome because the manner of relationship of parents was known there was an excess of males. When the reverse was true and the defect came to the father through the X chromosome, there was an excess of females. It is known, despite the fact that crossing over occurred twice in this family, that the defect was carried in the Y chromosome if the defect is partially sex linked. There were 9 boys and 5 girls, an excess of males. This is in accord with what was found in the other families.

There were six miscarriages, and it may be argued that had the sex of the fetuses been known it might have made a more even distribution of males and females. This may be true, but there is always an excess of males among miscarriages in general, hence it would seem likely that this family had been producing an excess of males. Taken alone, this might not be significant, but viewed in the light of the data furnished by the other families observed, it would seem that this family is conforming to the rule that more males, both normal and affected, are produced when the defect comes through the Y chromosome.

One more point may be made here. Had this family stopped somewhere short of the tenth child and had the manner of relationship of the parents not been known one might have assumed that it was through the X chromosome that the father received the defective gene, since there were 2 girls and only 1 boy affected and because one would expect crossing over to occur

less often than non-crossing-over. If the gene for this disease is incompletely sex linked, as Haldane<sup>4</sup> has maintained, crossing over occurred twice out of three times in the first group of this family. In the last three times in which the children were affected, all were boys and there was no crossing over of the defective gene. It may be that when the assumption has been made that the gene came through the father's male parent, because of an excess of affected males, or through the father's female parent, because of an excess of affected females, the assumption has not always been correct.

#### SUMMARY

Additional data have been supplied regarding the family reported on by Mayrand and Gaumond, which show that the father, who was first cousin to his wife, was related to her through his father, who was her maternal uncle. The defective gene came to him in the Y chromosome of his father, if xeroderma pigmentosum is incompletely sex linked.

There were 14 children in the family, 4 affected males, 4 unaffected males and 1 male who died at the age of 1 day. There were 2 affected females and 3 unaffected females. One of the unaffected daughters has married a first cousin, the son of her father's brother. There are as yet no offspring from this marriage.

Because 2 of the 6 affected persons were females, the crossing over value was 33.3 per cent.

Dr Emile Gaumond called my attention to this family. Mr Georges Lachapelle enlisted the assistance of his sister, sent me additional material and gave me permission to publish it. Dr Pauline Lachapelle made the trip to the home of the family and secured the additional information as to the mode of relationship of the parents and the data on the marriages in the fourth generation, together with the mode of relationship of two of the members who have married.

<sup>4</sup> Haldane, J. B. S. A Search for Incomplete Sex Linkage in Man. *Ann Eugenics* 7:28 (June) 1936.

# TREATMENT OF ICHTHYOSIS

CAPTAIN HYMAN H GORDON

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The results of treatment in 2 cases of ichthyosis in soldiers are presented in this paper

The report of Rapaport, Herman and Lehman<sup>1</sup> suggested a vitamin A deficiency as an etiologic factor of ichthyosis. High oral doses of vitamin A, 60,000 to 200,000 units daily, produced favorable clinical results in all the 6 patients treated. In 5 cases, biophotometric tests indicated vitamin A subnutrition. Rapaport suggested that the basis might be a hereditary disorder of vitamin A metabolism. Improvement with vitamin A was noted in one month and was progressive. When treatment was stopped there was regression. In 1 case in Rapaport's series there was no response to oral treatment, but considerable improvement was obtained with intramuscular injections of vitamin A. In this series bile salts did not improve visual dysadaptation.

Another plan of treatment was reported by Ljungstrom.<sup>2</sup> This author noted that in a patient with severe ichthyosis, sites of excessive perspiration were free of lesions. A treatment of daily baths in 3 per cent sodium chloride solution followed by application of 10 per cent sodium chloride in hydrous wool fat was able to keep the patient symptomless for five months.

My 2 patients were treated by these two plans, singly and combined. In addition, bile salts and neostigmine were used for the following reasons. Spector, McKhann and Meserve<sup>3</sup> reported that the absence of bile salts is a large factor in the interference with the absorption of vitamin A. Flax, Barnes and Reichert<sup>4</sup> showed that augmented absorption of vitamin A occurred when gastrointestinal motility and tone were

increased with neostigmine in the presence of cystic fibrosis of the pancreas. Popper, Steigman and Zevin<sup>5</sup> concluded that the plasma vitamin A levels are related to the efficiency of absorption from the intestine.

## REPORT OF CASES

CASE 1—A soldier aged 23 complained of an itching, dry, scaling skin, present as long as he could remember. The summer season was said to bring complete relief of symptoms, and improvement would be maintained by

## Results of Treatment

| Case | Date of Treatment | Kind of Treatment   | Result   |
|------|-------------------|---|--|
| 1    | 7/19 to 8/20/43   | Multivitamin capsules (20,000 units vitamin A)  | No improvement until 8/20/43, beginning desquamation                                 |
|      | 8/20 to 9/3/43    | 50,000 units vitamin A concentrate  | Decided improvement, with desquamation on thighs and arms                            |
|      | 9/3 to 9/17/43    | Same, discontinued 9/17   | No further change  |
|      | 10/25 to 12/6/43  | 100,000 units vitamin A daily discontinued 12/6   | Complete regression from September to October, slight improvement with 100,000 units |
|      | 4/6 to 4/10/44    | 100,000 units vitamin A, bile salts and neostigmine, daily 3% NaCl baths and 10% NaCl in hydrous wool fat | Decided desquamation   |
| 2    | 4/10 to 4/26/44   | Same, discontinued 4/26   | Improvement of 50% of ichthyotic area  |
|      | 7/11 to 7/31/44   | Daily 3% NaCl baths and 10% salt in hydrous wool fat (sweating formula)                                   | Good, clearing of arms, legs, abdomen  |
|      | 8/1 to 8/14/44    | 200,000 units vitamin A, bile salts and neostigmine   | Good, further clearing   |
|      | 8/14 to 9/1/44    | Combined of two preceding methods   | Complete clearing  |

going to warm climates in the fall and winter. The relief lasted sometimes for several years. No familial incidence was elicited.

Physical examination revealed a dry, scaly skin, generalized below the neck, but worse on the extensor surfaces of the arms and legs and around the waistline. The general health was unaffected.

Vitamin A in multivitamin capsules was given in a dose of 20,000 U S P units daily. From July 19 to July 30, 1943 there was no improvement. On August 20 there was slight improvement with beginning desquamation, and the administration of 50,000 units of concentrated vitamin A was started. Decided improvement.

5 Popper, H., Steigman, F. and Zevin, S. On Variations of Plasma Vitamin A Level After Administration of Large Doses of Vitamin A in Liver Disease, *J Clin Investigation* 22: 775-783 (Nov) 1943.

1 Rapaport, H. G., Herman, H., and Lehman, E. Treatment of Ichthyosis with Vitamin A, *J Pediat* 21: 733-746 (Dec) 1942, correction, *ibid* 22: 120 (Jan) 1943.

2 Ljungstrom, C. E. Eine einfache und wirksame Therapie bei Ichthyosis, *Acta med Scandinav* 108: 98-105, 1941.

3 Spector, S., McKhann, C. F., and Meserve, E. R. Effects of Disease on Nutrition: Absorption, Storage and Utilization of Vitamin A in Presence of Disease, *Am J Dis Child* 66: 376-395 (Oct) 1943.

4 Flax, L. J., Barnes, M., and Reichert, J. L. Vitamin A Absorption and Its Relation to Intestinal Motility in Fibrocystic Disease of Pancreas, *J Pediat* 21: 475-484 (Oct) 1942.

with desquamation on the thighs and arms was noted on September 3. Up to September 17 there was little further change, and by then the supply of vitamin A was exhausted. Treatment could not be continued until October 25. At that time there was a regression to the state prior to treatment, and 100,000 units of vitamin A was given. There was only slight improvement by December 6, and treatment was discontinued until April 6, 1944. On this date, 100,000 U S P units of vitamin A with 10 grains (0.65 Gm) of bile salts and neostigmine methylsulfate, 1/4,000, was given in addition to daily baths in 3 per cent solution of sodium chloride, followed by 10 per cent sodium chloride in hydrous wool fat. Four days later decided desquamation was noted. On April 26 a definite improvement of 50 per cent of the cutaneous area was estimated.

Thereafter, treatment was irregular. Regression would occur within a month after the stopping of treatment.

CASF 2—A soldier aged 19 reported with an eruption present since birth. The lesions were elevated, wartlike and brown pigmented. The skin intervening between the areas of horny nevus was dry and scaly. The diagnosis was *ichthyosis hystrix*. A younger brother had a similar disease.

Treatment was started on July 11, 1944. Daily salt baths and ointment were given. On July 31 the lesions had largely disappeared from the arms, legs and abdomen. On August 1 this sweating treatment was stopped, and vitamin A was given in doses of 200,000 U S P units daily with 10 grains of bile salts and 1 ampule of 1/4,000 solution of neostigmine methylsulfate.

From August 1 to August 14 further clearing of the *ichthyosis* occurred about as rapidly as with the previous sweating therapy. After August 14 a combined therapy was instituted, and by September 1, fifty-one days after treatment was initiated, all lesions had cleared. In the table are summarized the methods of treatment and the response in both cases.

#### SUMMARY AND CONCLUSIONS

Two types of successful therapy for *ichthyosis* have been developed: (a) the sweating treatment of Ljungstrom consisting of daily baths in 3 per cent sodium chloride solution followed by 10 per cent sodium chloride in hydrous wool fat and (b) vitamin A in high daily doses, up to 200,000 units, with bile salts and neostigmine.

It is felt that bile salts and neostigmine favorably influence the utilization of vitamin A and are valuable in the treatment of *ichthyosis* as well as other conditions accompanied with defective vitamin A metabolism.

Cessation of treatment in case 1 caused a regression in a short time.

In view of existing shortages of vitamin A, a simple and workable therapy for *ichthyosis*, the sweating treatment, can be an adequate substitute for vitamin A therapy.

# COLLOID DEGENERATION OF THE SKIN (COLLOID MILIUM)

REPORT OF A CASE, WITH OBSERVATIONS ON ASCORBIC ACID THERAPY

SAUL S. ROBINSON, M.D., AND SAMUEL TASKER, M.D.

LOS ANGELES

Colloid degeneration of the skin is a rare dermatosis. Only 24 authentic cases have been recorded since Wagner<sup>1</sup> first described the disease, in 1866. The case reports, pathologic features and nomenclature of colloid milium have been reviewed in recent articles by Way-Reuter and Becker<sup>2</sup> and Arnold.<sup>3</sup> Way,<sup>2</sup> in 1942, was the first investigator to report the use of ascorbic acid in the treatment of colloid milium in a patient who had laboratory evidence of vitamin C deficiency. After an attempted correction of this deficiency the cutaneous lesions disappeared. In his report, Way<sup>2</sup> stated that "the vitamin C deficiency existing in this case and the improvement seen following its attempted correction suggest that further studies may place this disease among the avitaminoses." Our patient with colloid degeneration of the skin received ascorbic acid therapy as suggested by Way. The favorable response of the lesions to ascorbic acid corroborates Way's observations and warrants this report.

## REPORT OF CASE

**History**—P. S., a 45-year-old Jewish man, operator of a parking lot, was first seen on Sept. 23, 1943, with the complaint that a papular eruption had been on the backs of his hands for over ten years. Similar lesions had recently appeared on his face. The papules have been indolent and persistent, slowly enlarging and spreading to involve almost the entire backs of his hands. There have been no subjective symptoms. There is no history of cutaneous disease in any other members of his family. The patient has a fair complexion and has worked outdoors in Los Angeles since 1921. This occupation constantly exposes his face, his neck and the backs of his hands to the heat and cold and to the actinic rays of the sun. The patient's health has otherwise been good.

Presented before the Los Angeles Dermatological Society, Oct. 12, 1943 (ARCH DERMAT & SYPH **49** 454 [June] 1944).

1. Wagner, E. Colloid-Milium of the Skin, Arch d. Heilk **7** 463, 1866.

2. Way, S. C. Colloid-Milium, Arch. Dermat. & Syph **45** 1148 (June) 1942.

3. Reuter, M. J., and Becker, S. W. Colloid Degeneration of the Skin, Arch. Dermat. & Syph **46** 695 (Nov.) 1942.

4. Arnold, H. L. Colloid Pseudomilium, Arch. Dermat. & Syph **48** 262 (Sept.) 1943.

**Dermatologic Examination**—There was an eruption with pinhead-sized to pea-sized papules located on the dorsa of the hands and on the malar regions of the face. The lesions were in groups of eight to ten. The individual papules measured 1 to 3 mm in diameter and were firm, translucent and yellowish white. When a papula was punctured, a clear mucoid, gelatinous liquid exuded. The skin on the dorsa of the hands, face and neck was rough and furrowed and tanned from exposure to the elements.

**Laboratory Examinations**—The Wassermann and Kahn tests of the blood elicited negative serologic reactions for syphilis. Examination of the blood showed hemoglobin content, 93 per cent, color index, 0.93, erythrocytes, 5,000,000, and leukocytes, 10,000, with 71 per cent neutrophils, 26 per cent lymphocytes, 25 per cent monocytes, and 0.5 per cent eosinophils. The cholesterol level was 277 mg per hundred cubic centimeters of plasma. The fasting sugar content was 103 mg per hundred cubic centimeters of plasma. The examination of the blood plasma for ascorbic acid showed 0.6 mg per hundred cubic centimeters, compared with the normal value of 0.7 to 1.4 mg. The ascorbic acid value rose to 0.8 mg per hundred cubic centimeters while the patient was receiving 500 mg of ascorbic acid by mouth daily.

**Histologic Examination**—A biopsy specimen from the dorsum of the right hand, stained with hematoxylin and eosin, showed a thinned epidermis with decided hyperkeratosis. In the papillary and subpapillary layers of the cutis were localized large masses of colloid replacing the collagen bundles. Large cells with nuclei were scattered sparsely throughout the clumps of colloid. The collagen fibers in other regions appeared swollen and separated. The accessory skin structures were normal. A section stained with Weigert's stain showed the elastic tissue to be sparse, swollen and discolored. Elastic tissue fibers were absent in the papillary and subpapillary layers of the cutis. No lipid was found in sections stained with sudan III. The microscopic diagnosis was colloid degeneration of the skin. The results of histologic examination agreed with those of previous reports of this disease. A second biopsy specimen was taken in February 1945, from a healed lesion adjacent to the biopsy specimen taken in 1943. A section of tissue stained with hematoxylin and eosin showed a thin epidermis with hyperkeratosis. Thick fibrous connective tissue was present throughout the upper and middle portions of the cutis, replacing the colloid masses. The elastic tissue was sparse, degenerated or absent throughout the healed areas. The diagnosis was scar tissue and atrophy of the skin.

The treatment consisted of a diet high in vitamin C, containing fruit, fresh vegetables and animal protein. The patient also received ascorbic acid in the dosage of 300 mg by mouth daily and 500 mg intravenously.

twice a week. Two months after this treatment was instituted, the papules on the face and dorsa of the hands began to disappear. One year later all the lesions except a few small papules on the back of the left hand had disappeared. Slight residual atrophic changes remained on the dorsum of the right hand at the sites of former papules. No recurrent or new colloid milium lesions have appeared since the administration of ascorbic acid. The patient had no toxic reactions attributed to the treatment.

#### COMMENT

Lanman and Ingalls<sup>5</sup> and Dalldorf<sup>6</sup> have shown, in experimental studies, the importance of vitamin C in regulating the development of collagen and the physical character of the intercellular fluid. Disturbance of the intercellular fluid in the colloid milium with degenerative vascular and perivascular changes was discussed by Way.<sup>2</sup> Exposure to the actinic rays of the sun may play an important role in the production of colloid degeneration of the skin, as in almost all reported cases of the disease there is localization of the lesions to the exposed surface of the face and hands. The hematoporphyrin content of the blood and urine has been within normal limits whenever reported. The hypercholesteremia observed in our patient is the fourth recorded instance of increased blood

5 Lanman, T. H., and Ingalls, T. Vitamin C Deficiency and Wound Healing. Experimental and Clinical Study, *Ann Surg* **105** 616, 1937.

6 Dalldorf, G. The Pathology of Vitamin "C" Deficiency, in *The Vitamins*, Chicago, American Medical Association, 1939, p. 389.

cholesterol found in association with colloid degeneration.

The attempted correction of a vitamin C deficiency in our case may account for the disappearance of the lesions. The patient did not protect his face or hands from the weather while receiving treatment. He also continued his regular occupation in the same locality. It is our opinion that the only factor that could account for the disappearance of the lesions is the administration of ascorbic acid. The treatment heretofore advocated for colloid milium in leading American dermatologic textbooks has been of a destructive character. Before Way's report on ascorbic acid therapy no successful attempt had been made to treat colloid milium on an etiologic basis. We are in agreement that the favorable response of this disease to ascorbic acid warrants further experimental study of colloid degeneration of the skin as a possible vitamin C deficiency disease.

#### SUMMARY AND CONCLUSIONS

Ascorbic acid was used successfully in the treatment of colloid degeneration of the skin (colloid milium).

This case presents the fourth recorded instance of hypercholesteremia associated with the colloid degeneration.

The disappearance of the patient's lesions during treatment with ascorbic acid, in an attempt to correct a possible vitamin C deficiency, justifies further study of colloid degeneration of the skin as a possible vitamin C deficiency disease.

1930 Wilshire Boulevard (5)

## Clinical Notes

### A FAILURE OF PENICILLIN IN THE TREATMENT OF GRANULOMA INGUINALE

#### Report of a Case

CAPTAIN JOHN R. HASERICK, MEDICAL CORPS, ARMY OF THE UNITED STATES

This is a report of an unsuccessful trial of penicillin in a case of granuloma inguinale. The attempt was made in the hope that a surer and quicker method could be found than the present regimen, which, though successful, requires prolonged treatment and careful watching for several months.

#### REPORT OF CASE

*History*—A private aged 22 was admitted to the medical service of a general hospital on April 15, 1944, to which he had been transferred from a field hospital. A penile lesion had appeared as a small papule on March 8, 1944, and it had gradually increased to the size and shape of a button with a diameter of 1 cm. His most recent sexual intercourse had been Jan 15, 1944. There was no pain with the lesion and no associated swelling. At the field hospital repeated dark field examinations showed no spirochetes and the Kahn reaction of the blood had been negative on several occasions. Treatment there had included two courses of sulfathiazole as well as sulfanilamide powder applied locally, with no effect on the lesion. The history by systems disclosed nothing significant. The past history revealed that the patient had had a similar lesion in the same location in May 1943 and was told that he had a "soft chancre." He received thirteen injections over a two month period, with the lesion gradually disappearing in the first two weeks of treatment. He was then inducted into the Army and received no further treatment.

*Examination*—The patient was well developed and well nourished. On his admission to the hospital his temperature was 98.4 F, the respiratory rate was 20, and the pulse rate was 76. The general physical examination was noncontributory. Examination of the genitalia revealed a flat round elevated red granulated papule in the right coronal sulcus. The papule measured 9 by 11 mm. It was moderately indurated and slightly tender. There was no adenitis.

Laboratory examinations revealed 14.6 Gm of hemoglobin and 7,000 white blood cells. Urinalysis, including a microscopic study, showed no abnormalities. Two dark field examinations showed no spirochetes. The Kahn reaction of the blood was negative. Scrapings from the penile lesion revealed abundant Donovan bodies. The Frei test elicited a negative reaction.

*Treatment*—Penicillin, (in a strength of 5,000 units per cubic centimeter in solution of sodium chloride) was administered intramuscularly in doses of 25,000 units every three hours for five days. The penicillin used in this case was Merck lot 131, of which the expiration

date was April 20, 1944. This lot was used simultaneously in 46 cases of sulfonamide-resistant gonorrhea, with excellent results.

Fifteen days after the penicillin had been administered there was no change in the lesion other than a slight increase in size and amount of granulation. Penicillin soaks in dilution 1 to 1,000, were then tried locally for four days. Soaks were used three times daily for one half hour. No effect was noted other than a change in the color of the lesion from red to reddish brown. Donovan bodies continued to be present in scrapings.

Twenty-two days after the administration of penicillin intramuscularly, there had been no improvement, the patient was given a course of fuadin consisting of 35 cc in divided doses over a twelve day period. There was an immediate response, and on the fifth day the lesion measured 6 by 9 mm. By the completion of the course the lesion measured 2 by 3 mm, and shortly thereafter it disappeared completely. The patient was discharged to duty, with further courses of fuadin to be administered by his unit dispensary.

#### COMMENT

The only untoward reaction noted during the administration of penicillin was a daily elevation of temperature (100 to 102 F), which began on the second day and ended on the fifth and last day. When the 1,000,000 units of penicillin had been administered, the patient's temperature dropped to normal and remained there the rest of his hospital stay.

The period of three weeks was allowed for observation because of the occasional delay in resolution in granuloma inguinale noted when the known effective substances, antimony and potassium tartrate and fuadin are used. The results, however, immediately following the use of the latter were striking in this case. While no deduction can be made from 1 case, it is indicative that penicillin failed to cause any response in a relatively mild infection of granuloma inguinale.

#### SUMMARY

A case was encountered in which granuloma inguinale failed to respond to 1,000,000 units of penicillin given intramuscularly and to four days' treatment with penicillin locally. Further treatment was delayed for three weeks for purposes of observation, with no improvement noticeable in the lesion. Immediate resolution of the disease followed the administration of fuadin in the usual dosages.

## Obituaries

### JAMES THOMAS WAYSON, M D

1870-1945

Dr James Thomas ("J T") Wayson died of bronchial pneumonia on Jan 12, 1945, at the age of 74, after more than fifty years of work in the fields of dermatology, leprology and public health in the Territory of Hawaii

Dr Wayson was born in Port Townsend, Wash, and came to Hawaii in the United States Revenue Cutter Service on Nov 25, 1894 In the following year he became superintendent of Kalihi Leprosarium, where he remained for two years, after which he relinquished this post to enter private practice In 1910 he again assumed charge of Kalihi Leprosarium, a post he held until 1915, when he exchanged it for the position of sanitary expert with the Board of Health In 1921 he was promoted to general health officer, and in the same year he became assistant administrator of the Board of Health, a position he held until 1931

In 1931, when the control of the territorial leprosariums at Kalihi and Kalaupapa was removed from the board of health and vested in a separate agency, the Territorial Board of Leper Hospitals and Settlement, Dr Wayson became chief physician of this board He held this post until his official retirement, in September 1943 At the time that he assumed office, the whole problem of the control of leprosy was in a turmoil, diagnoses were often contested, sometimes in court, for segregation was extremely unpopular Little attention was being paid to cases in which the diagnosis was already made, and scant effort was being exerted to follow up paroled patients It was in large part owing to Dr Wayson's efforts and to those of the first members of the board that the "lepei" came to be regarded as a "leprous patient" and was given some measure of sympathy and personal attention, instead of the simple confinement that had previously been the rule

One of Dr Wayson's chief accomplishments was the establishment of an inconspicuous, seemingly private office, in a quiet part of town, for the periodic examination of parolees and the examination of suspects and for rendering general medical care to these persons and to their families

Dr Wayson was among the first physicians, if not the first, to use solid carbon dioxide for the reduction of lepromas, he reported this work to the Territorial Board of Health in 1912

Dr Wayson was made an honorary member of the Honolulu County Medical Society in 1932, he was a member of the Hawaii Territorial Medical Association and a Fellow of the American Medical Association He was a charter member of the American Academy of Dermatology and Syphilology, and he belonged to the Society for



JAMES THOMAS WAYSON, M D

1870-1945

Investigative Dermatology and the Royal Society of Tropical Medicine and Hygiene He was a charter member, and the first president, of the Hawaii Dermatological Society He was a Mason, an Odd Fellow and an Elk Most important, he was a kindly, friendly, witty and wise practitioner of dermatology and student of leprosy he would not call himself a "leprologist" He will long be remembered and missed by his many acquaintances and still more numerous friends, on the mainland and in Hawaii

HARRY L. ARNOLD JR M D



## Correspondence

### PENICILLIN IN THE TREATMENT OF CUTANEOUS DISEASES

*To the Editor* —I have noted that several observers have reported their results in the treatment of pyogenic dermatoses with penicillin in an ointment base. Inasmuch as I have been using a penicillin-containing ointment ever since October 1943 and have treated many hundreds of patients with this material, the following statement might be in order. After experimentation I have found that 800 units of penicillin per gram of vehicle is the most effective dose. The best vehicle was found to be a petrolatum-cholesterol ointment base (Aquaphor), when it is possible to obtain it. One of my most disappointing discoveries has been that sycosis vulgaris does not respond effectively to penicillin ointment, and to date I have treated about 30 patients with that disease. The results in treatment of impetigo contagiosa, as noted by others, are startling, and I have had patients with this disease who got well in twenty-four hours. The only "eczemas" which I feel respond are those which are secondarily infected. Penicillin was absolutely of no value for the cystic and pyogenic types of acne vulgaris, of which I have encountered many cases. In cases of acne vulgaris the patients for the most part not only did not do well in the Pacific but became definitely worse, and in many cases the first lesions appeared after the end of the period of adolescence. Penicillin was of no value in the treatment of fungous diseases except in those cases in which the lesions were secondarily infected. Peculiarly, pyogenic infection about the ears and eyes responds well, and I use this drug almost as a specific treatment for such infections. Furunculosis does not respond so readily, and when treated by the intramuscular method huge amounts of penicillin must be given. One patient, whom I recently treated, received 5,000,000 units before the disease was controlled.

Penicillin has been of little value in the treatment of chancroid except in those cases in which there is secondary spirochetal infection. This applies to cases in which penicillin has been administered either intramuscularly or locally. These results are to some extent slightly different from those reported recently in the *Journal of Investigative Dermatology*. Several cases of granuloma inguinale which I have treated with penicillin both intramuscularly and locally (1 of which has been reported) failed to respond to penicillin. In 1 case of actinomycosis which I treated large amounts (5,000,000 units to be exact) of penicillin were required before the disease was cured clinically.

CAPT LAWRENCE C GOLDBERG, M C, A U S

Chief of Dermatology Section, Oliver General Hospital, Augusta, Ga

### TREATMENT OF PITYRIASIS ROSEA WITH TRICHOPHYTON EXTRACT

*To the Editor* —I was much interested in Dr Ilona Vass's article, "Treatment of Pityriasis Rosea with Trichophyton Extract" (ARCH DERMAT & SYPH 51 203 [March] 1945), because it stated that intradermal

injections of trichophyton extract were of benefit in the treatment of pityriasis rosea. It was found that when this extract was so administered three times weekly for three to six injections of a 1:500 dilution there was a decided improvement in the majority of patients, whereas a 1:30 dilution of the same extract injected into the skin produced a temporary aggravation of the eruption in others. For these reasons the author concluded that the theory of a fungous origin of pityriasis rosea was favored.

Goodman (ARCH DERMAT & SYPH 25 873 [May] 1931) raised the question of this possible relationship because of a series of positive reactions to trichophyton which he obtained in patients with the disease, but he also found a similar hypersensitivity to the extract in patients with acne. Furthermore, Van Dyck, Kingsbury, Thorne and Meyers (New York State J Med 31 611 [May 15] 1931) tested a series of patients suffering with pityriasis rosea and obtained positive reactions in all their patients. I was also interested in the possible fungous cause of pityriasis rosea (ARCH DERMAT & SYPH 25 847 [May] 1932) and similarly investigated a series of patients with this disease. Intradermal injections of 1:20 and 1:50, trichophyton extract of known potency to which no preservative had been added were used. In addition, the diluted extract was cultured daily to be sure that there were no viable bacteria present that might produce a false positive reaction. By this method it was found that 21 of 29 patients with pityriasis rosea had negative reactions to the intradermal tests. Of the remaining 8 whose reactions were positive, it was found that a clinically typical fungous infection of the feet was present in each, and in 5 of these patients hyphae were observed by microscopic examination of the affected scales in potassium hydroxide preparations.

I suggest that the rapid improvement reported by Dr Vass in these patients was due to daily starch baths and loose clothing prescribed or, as was suggested in the article, to a possible nonspecific effect of the trichophyton extract. However, from my studies previously cited I am of the opinion that pityriasis rosea cannot be considered a fungous infection.

LIEUT COMDR C C CARPENTER (MC), U S N R

### THE EFFECTIVE THREE HOUR TREATMENT OF SCABIES

*To the Editor* —In a recent issue of the *Military Surgeon* (96 271 [March] 1945), Major Simon Rubin and Captain Harvey Blank published an article entitled "The Effective Three Hour Treatment of the Scabetic Patient." They used the method which Dr Henry A. Smith and I recommended (ARCH DERMAT & SYPH 48 370-372 [Oct] 1945).

I introduced this treatment during World War I in the Austrian Army and after the war in the civilian population. About 70,000 patients with scabies were thus treated. It might be of value if this method were to receive more attention in the treatment of soldiers and civilians.

MAURICE OPPENHEIM, M D, Chicago

25 East Washington St

## THE USE OF METHENAMINE IN DERMATOLOGY

To the Editor —Dr Erich Urbach, of Philadelphia, in his letter on "Erythema Multiforme Its Relationship to Herpes Simplex" in the ARCHIVES (51 228 [March] 1945) suggests the use of methenamine to shorten the course of herpes labialis and erythema multiforme. He mentions a case (with photograph) in his book on allergy (New York, Grune & Stratton, Inc., 1943, p 902) of the occurrence of both herpes labialis and erythema multiforme in the same patient.

Since a noted dermatologist and allergist from a great medical center writes a special letter concerning his successful treatment of herpes and erythema multiforme with methenamine, readers of the letter may assume that this is a new form of treatment, as no references to previous reports of its use are included in Dr Urbach's letter.

May I call attention to the early reports on the use of methenamine in the therapy of herpes labialis, herpes zoster and erythema multiforme? In 1929, while I was doing postgraduate work in Vienna, and again in 1931 and 1932, my friends Dozent Stephan Robert Brunauer and Prof Maurice Oppenheim suggested to me the value of methenamine in the treatment of these dermatologic diseases. Alfred Perutz (1930), of Vienna, O Hirschmann (1926), Kotiers (1931), of Vienna, Otto Sachs (1912, 1916, 1919), Chlamow (Russian), Walthier Schonfeld (1928), of Greifswald, Hauer (1931), of Nienburg, R von Leszczynski (1931), Coglievina (1924), H I Goldstein (1929, 1930, 1931), of Camden, N J, Brunauer, Oppenheim, and C J White have previously reported the use of methenamine in the treatment of dermatologic diseases, including herpes zoster, erythema multiforme and erythema nodosum, pemphigus (von Leszczynski) and trichophytic infection (O Sachs). C J White found hexamethylenamine helpful in the treatment of erythema multiforme.

This is a matter of rendering "unto Caesar the things which are Caesar's." I am appending here pertinent references to the literature. I might add here that I reported 2 cases of streptococcic sore throat with erythema multiforme and erythema nodosum treated with methenamine (long before the days of penicillin, streptomycin and the sulfonamide compounds!) at the thirty-

second annual meeting of the American Therapeutic Society, held in Atlantic City, N J, June 5, 1931, and before the Camden (N J) County Medical Society (1930).

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HYMAN I GOLDSTEIN, M D, Camden N J

### CORRECTION

In the report of the Atlantic Dermatologic Conference in the July issue (*ARCH DERMAT & SYPH* **52** 39, 1945) the title of the report presented by Dr. Frank J Eichenlaub (second column, page 49) is incorrect, it should read "Granuloma Inguinale" instead of "Mycosis Fungoides."

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

## PSEUDOCARCINOMATOUS HYPERPLASIA IN PRIMARY, SECONDARY AND TERTIARY CUTANEOUS SYPHILIS HERBERT LAWRENCE, Arch Path, 38 128 (Sept) 1944

Lawrence states that it is necessary to be constantly alert to the possibility of pseudocarcinomatous hyperplasia occurring in granulomas and chronic ulcers of the skin. When all criteria are taken into account, it may still be difficult to distinguish carcinoma and pseudocarcinomatous hyperplasia by study of the histologic section alone. With syphilis the process is likely to occur most frequently in cases in which pseudocarcinomatous hyperplasia is superimposed on a gumma. Three cases are presented as offering illustrations of pseudocarcinomatous hyperplasia occurring in persons with primary, secondary and tertiary cutaneous syphilis.  
LYNCH, St Paul

## DEATH CAUSED BY VACCINIA IN AN ECZEMATOID INFANT CARL L. PETERSILGE and JOHN A. TOOMEY, Arch Pediat 61 455 (Sept) 1944

The case of an 8 month old white baby boy with eczema, who was accidentally and indirectly vaccinated with smallpox from contact with the pustule of an older sister, is reported. The sister had been previously vaccinated against smallpox. The infant had always been well except for an uncomplicated eczema present since birth. Nine days after the exposure to the pustule, umbilicated vesiculopustular lesions, varying from 5 to 10 mm in diameter, developed on the face and head. There were lesions on the face, head, eyelids and in the nares. Within forty-eight hours the eruption appeared on the extremities. The child became progressively more toxic and died on the eleventh day.

The report includes the hospital course, postmortem observations and microscopic description of the lesions.

GELBER, Los Angeles

## SYMPTOMATIC NEUROSYPHILIS HARRY C. SOLOMON, J. E. MOORE, PAUL A. O'LEARY, JOHN S. STOKES and E. THOMAS, Bull U S Army M Dept, October 1944, no 81, p 55

The authors briefly discuss the symptoms and pathologic changes of neurosyphilis. The clinical manifestations are discussed under the following main headings: (1) meningeal neurosyphilis, (2) meningovascular neurosyphilis, (3) tabetic neurosyphilis, (4) parietic neurosyphilis, (5) vascular neurosyphilis and (6) congenital neurosyphilis. Various relatively rare and controversial syndromes, such as chronic anterior poliomyelitis, parkinsonism and disseminated sclerosis-like pictures, are only mentioned but not discussed.

## THE TREATMENT OF NEUROSYPHILIS H. C. SOLOMON, J. E. MOORE, P. A. O'LEARY, J. H. STOKES and E. W. THOMAS, Bull U S Army M Dept, November 1944, no 82, p 66

The authors discuss the following agents in the treatment of neurosyphilis: (1) trivalent arsenical compounds and bismuth preparations, (2) trypanamide, (3) penicillin (only mentioned) and (4) induced fever,

including (a) malaria, (b) artificial elevation of temperature, sometimes combined with chemotherapy, and (c) elevation of temperature from typhoid vaccine. The treatment of special forms of neurosyphilis is discussed only briefly. Finally, the results to be expected of treatment with the agents mentioned, especially with fever therapy, in the various stages of neurosyphilis are considered.

## TRENCH FOOT J. C. EDWARDS, M. A. SHAPIRO and J. B. RUFFIN, Bull U S Army M Dept, December 1944, no 83, p 58

The authors discuss the symptoms and course of trench foot. The treatment used by the authors consisted of cool water soaks and whirlpool baths at 70 F for twenty to thirty minutes daily. The feet were washed daily with soapy water, of 70 F, and the surface of the feet was cooled by air currents from a fan or by exposing the feet to room temperature not exceeding 70 F, but preferably about 50 F. One hundred and fifty to 300 cc of 5 per cent solution of sodium chloride, administered intravenously daily, often gave immediate symptomatic relief from aches and pains.

In their conclusions, the authors emphasized that all patients with trench foot should go through a rehabilitation period of at least two weeks of daily hikes before returning to duty.

STRAKOSCH, Denver

## ERYTHEMA NODOSUM IN CHILDREN EDITH M. LINCOLN, JANET ALTERMAN and HYMAN BAKST, J Pediat 25 311 (Oct) 1944

The total number of cases of erythema nodosum encountered in three large hospital services in the United States is small compared with the numbers reported from northern continental Europe. In the majority of adolescent and adult patients seen in Boston and New York the eruption would seem to be due to infections other than tuberculosis. In the series reported from the children's ward of Bellevue Hospital, New York, 74 per cent of the children with erythema nodosum reacted positively to the tuberculin test, three to four times the normal incidence, although for only 39 per cent of them could tuberculosis be considered definitely responsible for the erythema nodosum. Of 362 patients over 2 years old with active primary tuberculosis, erythema nodosum occurred in 36 per cent. The symptom complex of erythema nodosum developed concomitantly with the primary tuberculosis in 27 per cent of the patients. It is possible that the apparent contradiction in medical literature concerning the causation of erythema nodosum may be due to the describing of groups of patients of varying ages. The authors of the present article conclude that every child with erythema nodosum should be regarded as potentially tuberculous but that no child should be finally considered tuberculous without a complete study, that when erythema nodosum occurs in children with active tuberculosis it is commonly associated with the early phases of the disease, and that erythema nodosum may be an important aid in the diagnosis of tuberculosis in an individual case. In the United States the disease

occurs so uncommonly that its usefulness as a diagnostic aid is much less than in northern Europe

AUTHORS' SUMMARY [Am J Dis Child]

CONGENITAL, HEREDITARY LYMPHEDEMA (MILROY'S DISEASE) KURT GLASER, J Pediat 25 337 (Oct) 1944

The author describes 2 cases of Milroy's disease observed at the Milwaukee Children's Hospital and gives a brief review of the entire subject, including the high lights of the literature

A disease, most likely Milroy's disease, was first described by J Hille, in Germany, about the middle of the last century and was again described by Milroy in 1890 in the United States Osler gave it the name Milroy's disease In 1928, after thirty-five years of observation, Milroy himself published a report about the same family he had described in 1892 and discussed the condition in general

The condition is defined as congenital hereditary edema without tenderness or painfulness and without constitutional symptoms It is of rare occurrence and usually affects several members of the same family The cause is unknown, and several theories have been suggested The symptom is pitting edema of one or both legs, never extending above Poupart's ligament There are no significant laboratory findings The pathologic microscopic manifestations are enlarged lymph spaces with increase in the surrounding fibrotic tissue The course is chronic and progressive The treatment is palliative It consists of applying pressure bandages to prevent further swelling

A white boy, aged 4 years at the time of this report, and his sister, one year younger, are described Both children had had swelling of the feet since birth The extent of the swelling varied, being influenced to a slight degree by the amount of exercise and by the application of pressure The boy showed a swelling of the prepuce, which was remedied by circumcision

Complete laboratory study of the urine, the chemistry of the blood (chlorides, nonprotein nitrogen, cholesterol, calcium, phosphorus, phosphatase, total protein and albumin and globulin) and the serologic reactions of the blood, as well as the wheal absorption test, gave normal results

Roentgenographic studies showed normal formation of bones in both children Microscopic examination of the boy's foreskin revealed large structures resembling lymphatics and dense collagen fibers, a picture typical of the disease as described by other authors

The treatment consisted of application of bandages of different types, all with the purpose of reducing the amount of edema by pressure The result was, as was expected, only slight and of temporary value

The paper reports 2 typical cases of Milroy's disease, demonstrating the absence of a causative constitutional disorder It describes the histologic characteristics of this disease, throwing some light on the theories of causation Two photographs show the edema of the legs

GLASER, Milwaukee [Am J Dis Child]

DIRECT CURRENT COMBINED WITH X-RAY THERAPY CASE OF KAPOSI SARCOMA THUS TREATED HARRY SIGEI, Radiology 43 386 (Oct) 1944

A patient with hemorrhagic sarcoma of Kaposi was treated with roentgen ray therapy combined with galvanic current applied locally to the lesions A better clinical response was obtained with combined treatment than was achieved on control lesions treated with roentgen ray therapy alone

HENSCHEL, Denver

FACTORS INFLUENCING DERMATITIS IN COAL MINERS R B KNOWLES, Brit M J 2 430 (Sept 30) 1944

The chief factors causing and influencing the nature of dermatitis in coal miners are (1) conditions in the pit such as (a) ventilation, temperature, humidity, height of the coal face and distance of the coal face from the shaft, (b) presence of water and the substances dissolved in it and (c) quantity, quality and state of subdivision of dusts and the effect of machinery on these, (2) the mental and physical constitution of the workmen, such as (a) behavior in relation to trauma and infection and (b) presence of tendencies toward seborrhea, hyperhidrosis or ichthyosis, which may predispose to dermatitis, (3) friction between cutaneous surfaces or between clothes and the skin, (4) use and abuse of cleansing agents and popular cutaneous applications in general

The chief points in prophylaxis are (1) adequate ventilation of the pit, (2) reduction in the quantity of dust to a minimum, (3) removal of water if possible, by pumping, (4) education of the personnel by means of (a) notices posted at the pit asking the men to report any suspected dermatitis at its onset, (b) instruction of ambulance attendants regarding treatment of patients with dermatitis, such as the correct method of application of protective lotion, (c) warnings as to possible deleterious effects from unsuitable cleansing agents and home remedies (good soaps, vegetable oils and liquid petrolatum allowed) and (d) emphasis on the advantages of cleanliness, (5) selection of suitable personnel for work in the pit, (6) application of protective substances to the skin, (7) warnings as to the increased risks of working when ill or insufficiently recovered from illness and (8) prevention of fungous infection of the feet by (a) examination of new workers before they are admitted to the baths, (b) prevention of contact between the feet and the bath floors, through use and periodic sterilization of bath slippers and (c) provision of separate baths for infected men

SUPERFICIAL GANGRENE IN ADOLESCENT DIABETES H WHITAKER, Brit M J 2 469 (Oct 7) 1944

Three examples of superficial gangrene in young persons with diabetes are reported The first patient was a boy 15 with diabetes of three years' duration, who was admitted to the hospital in coma Despite good nursing attention, a large area of gangrene involving the right buttocks suddenly appeared, which later became secondarily infected

The second patient was a soldier 24 years old, who was admitted to the hospital in coma An area of dry superficial gangrene developed on the anterior surface of each knee The shape and symmetry suggested that they were due to pressure of the bed clothes Healing required six weeks

The third patient was a 29 year old man, who by mistake injected insulin intradermally instead of subcutaneously, there resulted small round patches of dry superficial gangrene at the sites of injection

MEDICAL EXPERIENCES IN NORTH AFRICA 1943-4 T C HUNT, Brit M J 2 495 (Oct 14) 1944

In a review of medical experiences in North Africa the author discusses several diseases of interest to the dermatologist In both the Middle East and North Africa, faucial, nasal and cutaneous diphtheria were important causes of sickness, of prolonged stay in the hospital and of serious complications or death

Cutaneous diphtheria is difficult to distinguish, since only a few of the lesions show characteristic features, which may be in the form of ulcers, superficial weep-

ing or crusting dermatitis or purulent injections of wounds, abrasions, burns or superficial injuries

The lesions are all slow to heal, the average duration of the disease before diagnosis was fifty days, and the average stay in the hospital before healing was thirty-five days. Autoinfection from hand to mouth or vice versa is of rather frequent occurrence. Severe polyneuritis following chronic cutaneous diphtheria was often seen, beginning between six and ten weeks after the cutaneous lesions were first noticed.

A LABORATORY TEST FOR DIAGNOSIS OF SMALLPOX  
C E VAN ROOYEN and R S ILLINGWORTH, Brit  
M J 2 526 (Oct 21) 1944

The authors have confirmed Paschen's observation that the elementary bodies of variola are larger than those of varicella and have utilized this finding to form the basis of a laboratory test for the identification of smallpox.

The laboratory and clinical findings corresponded in 96 per cent of 80 cases of smallpox. A negative result was returned in 3 cases. In no instance did a positive laboratory verdict disagree with the final clinical diagnosis of the case. The test is not applicable to the diagnosis of chickenpox.

The principal conclusion reached is that the method can be of great value in the early recognition of smallpox, especially on the first day of the eruption, when the clinical picture may so closely simulate that of chickenpox.

AETIOLOGY OF ERYTHEMA NODOSUM C BRUCE PERRY,  
Brit M J 2 843 (Dec 30) 1944

Perry studied a series of 112 cases of erythema nodosum in an attempt to determine the causation in each. There was a preponderance of women, 76 as against 34 men. Sixty-one patients reacted positively and 51 negatively to the Mantoux test with 0.01 mg of tuberculin.

Of the subjects with positive Mantoux reactions, the author believes that 32 were definitely tuberculous and 28 were probably tuberculous. The 51 with negative Mantoux reactions he regards as certainly not tuberculous. Analyzing the age groups, the author noted that of patients under the age of 15 tuberculosis was definite or probable in 72 per cent, whereas in those over 15 tuberculosis was definite or probable in only 23 per cent.

The review does not support the theory that erythema nodosum is a manifestation of acute rheumatism. The author believes that erythema nodosum must be re-

garded as a result of a nonspecific reaction to a variety of infectious or toxic agents and that it is not a specific disease. However, there is apparently a constitutional predisposition to the disease, since frequently several members of a family suffer from erythema nodosum. There is also evidence that endocrine factors contribute to this predisposition.

SHAW, Chattanooga, Tenn

LICHEN PLANOPILARIS CLOVIS DE CASTRO, Arq de  
dermat e sif de São Paulo 6 101 (July-Dec) 1943

De Castro describes a case of lichen planus in a woman aged 35, who in addition to the typical plane papules had interspersed among them acuminate perifollicular lesions. The histopathologic changes in the acuminate lesions resembled those of lichen planus, with the addition of follicular dilatation and a cornified follicular plug.

The earlier writings on this subject are discussed, and the author concludes that "lichen planus et acuminate" of the French, or lichen planopilaris (Pringle), is an entity—that it is a form of lichen planus and not the simultaneous occurrence of two diseases.

CLINICAL CONCEPT OF BRAZILIAN PEMPHIGUS FOLIACULUS ULYSSES L TORRES, Arq de dermat e sif de São Paulo 8 86 (June) 1944

According to Torres, the bullous phase of Brazilian pemphigus foliaceus occurs with an acute onset, followed by a chronic exfoliative phase. There then occurs a cachectic phase, and the cutaneous symptoms often subside before death.

According to the author, the disease should be called Brazilian pemphigus foliaceus rather than pemphigus foliaceus, as described by Cazenave, from which it differs in its intensely bullous onset, the absence of lesions on the mucous membranes and the predilection for adolescents and young adults. Abortive forms occur and the mortality of the Brazilian form is 80 to 90 per cent.

The disease is of major importance in Brazil, being endemic in certain areas, whereas the European form is uncommon and sporadic. The differences may be climatic, and it would be plausible to speak of it as "tropical pemphigus foliaceus."

Reports of 13 cases, with photographs, are included. The author theorizes that the cause may be an infectious agent and the cutaneous manifestations may be various phases of allergy or anergy due to the noxa.

STEVES, Minneapolis

# Society Transactions

## PHILADELPHIA DERMATOLOGICAL SOCIETY

CARROLL S WRIGHT, M D, *Chairman*

CARMEN C THOMAS, M D, *Secretary*

*March 17, 1944*

### Generalized Calcinosis Cutis Without Involvement of Muscles or Nerves Presented by DR HENRY B DECKER and DR A G PRATT

T M, a white boy aged 5 years, presents nodules varying in size from 0.5 to 8 cm. Some are hard, fixed to the skin and immovable, others are soft and movable. There are ulcerated nodules and depressed scars localized on the forearms, arms, legs, thighs and buttocks, with the ulceration and scarring particularly noticeable at the joints. One small nodule is present on the left side of the face. The child's weight at birth was 7 pounds 6 ounces (1,985 Gm). He was bottle fed with cow's milk. He had malaria on the arms when he was 4 months old. He has had measles and a few colds but no other illnesses. Hard lumps appeared under the skin of the right arm when he was 18 months old. At 2 years of age similar lumps appeared on the left arm. A physician then advised that the child be given two glasses of milk with each meal, because of undernourishment. Since that time hard lumps have continued to develop on the extremities and buttocks. One recently appeared on the left side of the face in the mandibular region. A blood count showed 78 per cent hemoglobin, 4,100,000 erythrocytes and 32,000 leukocytes, with 85 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes and 1 per cent eosinophils. The serum calcium level was 11 mg per hundred cubic centimeters, phosphorus level, 4 mg and phosphatase activity, 4 units. The Wassermann reaction of the blood was negative. The urine was normal. Biopsy disclosed calcium deposits in the skin. The patient has been given sodium biphosphate, with unquestionable clinical improvement, i. e., cessation of drainage, healing of ulcers, softening and apparent decrease in the size of the masses. Roentgen studies in December 1943 and February 1944 showed similar conditions.

#### DISCUSSION

DR ARTHUR G PRATT, Camden, N J. It may be that the improvement is more apparent than real. When the child first came into the clinic he walked uncomfortably and sat down gingerly, as if afraid to move. One reason was that on one buttock there was a mass about the size of an orange, which was draining at that time, hence, he had reason for sitting down carefully. On the elbows and the knees there were draining sinuses which have healed, and the masses have softened so that one can now feel the muscles underneath. But whereas the child is clinically improved, the roentgenologist was unable to see much difference in the actual amount of calcium present in the tissues at a second reading. We shall repeat the roentgenograms later and hope that they will show improvement in addition to the clinical evidence. I might also say that in looking up the subject we found an account of one child who recovered spontaneously.

DR CARMEN C THOMAS. We have had under observation for five years a patient with calcinosis whose serum calcium level has been normal. She is spontaneously recovering, has been discharging some of the calcium deposits, and no new lesions have developed.

DR HENRY D DECKER, Camden, N J. When we first saw this child there was a question whether we were dealing with a juvenile xanthoma, because the lesions had a yellow color. We wondered, therefore, whether there was not a defect in the fat metabolism and the calcium deposit resulted from that.

DR ISADORE ZUGERMAN. Are there any deposits in the organs—in the kidneys, for example?

DR ARTHUR G PRATT, Camden, N J. We have had roentgenograms taken of the entire body—skull, extremities and trunk—and the roentgenologist says that all the calcium deposits are in or under the skin and not in muscles, nerves or in other structures. While making the biopsy we encountered an unusual grayish white liquid, like a suspension of flour or fullers' earth and water. We had selected a small and, as we thought, discrete nodule and cut well around it, but in doing so we cut into one of these chains of deposits.

DR FRED D WEIDMAN. I take it that there is no question about the diagnosis. The only thing I can discuss, perhaps, is the nature of this soft, fullers' earth-like material. There is a possibility that it is composed largely of soaps. In the pathogenesis of calcification in general, it often happens that, preceding the calcification, soaps are laid down for one reason or another. At first they are neutral, soluble soaps. Later they combine with calcium to form insoluble calcium soaps. I imagine that at this stage, in a finely subdivided condition, they would still not be gritty but perhaps like the fullers' earth mentioned. Only later, after the granules have coalesced, would a definite grittiness be experienced. This could be tested by securing a fairly large sample of the fullers'-earth-like material, shaking it up with an excess of water and finding out whether it dissolves. It could then be evaporated to learn whether the same kind of fullers'-earth-like material develops. Of course there are special microchemical tests for soaps that could also be applied. In this case there is a highly interesting lead in connection with the pathogenesis of calcinosis cutis. Thus, of course, the calcium is in the forefront as one sees these cases clinically, but, after all, the calcium is only the terminal stage, what one would like to know more about is the stages intermediate between the faulty action of the parathyroids and the eventual laying down of calcium in the tissues. Accordingly, this case may be an indication that the role that the parathyroids play may be not in the direction of upset calcium metabolism but of soap metabolism, this, in turn, would imply fat metabolism.

### Lichen Scrofulosorum and Tuberculosis Colliquativa Presented by DR JOHN F WILSON

A M W, a white woman aged 52 years, presents erythematous nodular lesions on the lower sides of the neck and the right side of the chest with ulceration of the center surmounted by a yellowish crust. Beneath the left breast there are scars of previously healed

lesions. On the back and on a few areas on the chest there are scattered, grouped, reddish and brownish red pustular lesions. Some are scaly and others crusted. In August 1942, the patient was sent to another hospital for study. Many roentgenograms were made and she was operated on for a floating kidney. She has lost about 20 pounds (13.6 Kg) since that time. She has had a cough for three or four years which has been worse recently. There are occasional pains in the lower part of the chest. In 1936 she had a boil-like lesion of the lower right side of the neck. This cleared, and the next developed four or five months later. Since then she has had many others, and she has had more frequent lesions. A roentgenogram of the chest showed bilateral pulmonary tuberculosis.

#### DISCUSSION

DR CARMEN C THOMAS: Have any tuberculin tests been done on this patient?

DR JOHN F WILSON: No. She has a bilateral pulmonary infection which is probably active. Examinations of the sputum have not revealed tubercle bacilli.

DR FRED D WEIDMAN: I should like to ask the other members whether in their opinions these lesions appear unusually acute for any kind of tuberculids—a bright red instead of dusky. Could these papular lesions be of the nature of bacteriids instead of tuberculids?

DR HENRY B DECKER, Camden, N. J.: These lesions are acute, and their course is short. They ran a course of about six weeks, which is characteristic of a tuberculid rather than of an infectious lesion.

DR FRED D WEIDMAN: Some years ago I made a visit to the New York Skin and Cancer Hospital, where a rather intensive study of acnitis was in progress, and I recall that it was Dr. Thorne's feeling that there was not a tuberculous causation in all cases, that in some, at least, there was a bacterial causation.

#### Keratosis Palmaris et Plantaris Presented by DR EDWARD F CORSON

A B, white man aged 23 years, presents thickened, yellowish brown hyperkeratoses on both palms and soles. The disease has been present as long as the patient can remember. He has no knowledge of his antecedents, but his son, now 7 months of age, has exhibited the same disease since shortly after birth. He has received a single roentgen ray treatment of 150 r to each palm, salicylic acid ointment, thiamine hydrochloride and thyroid.

#### Urticaria Pigmentosa with Sensitiveness to Temperature Presented by DR ARTHUR G PRATT, Camden, N. J.

J S, a white woman aged 20, presents sharply margined, brown, oval macules, 0.5 to 2 cm in diameter, scattered thickly over the extremities and more sparsely on the trunk. A few dull red wheals are present on the legs and forearms. When the patient was 9 years of age, a few itchy welts resembling mosquito bites appeared. These quickly subsided, leaving brown macules. New lesions have appeared continuously during the past eleven years. The pigmented macules seem to fade in the summer. When the body is chilled the most recent spots tend to become itchy, red and elevated. The patient has always enjoyed good health, and there are no other instances of pigmentation in her family. She is unusually sensitive to variations

in temperature, her hands are uncomfortable in hot water, and exposure to cold affects her more than it does the ordinary person.

#### DISCUSSION

DR MORRIS MARKOWITZ: Histologic examination would be of importance. It should show an excess of mast cells, which would settle any question as to diagnosis.

#### A Case for Diagnosis (Dermatitis Herpetiformis?) Presented by DR EDWARD F CORSON

H E, a white man aged 59 years, at the age of 14 years had a blister on his face. This ruptured, and other lesions formed where the fluid had spread on the skin. This lesion never cleared entirely, there were intermittent attacks until the age of 20, when the perianal region also became involved. He has had burning on urination for over thirty years, accompanied with a urethral discharge. Several years ago he was thought to have diabetes, as he exhibited polyuria, craving for water and the loss of 26 pounds (11.8 Kg) of weight in a year. Results of dextrose tolerance and other tests were normal, however. Because of pain in the leg he was studied in the vascular clinic. A roentgenogram of his leg was made, and a calcified artery was apparent. He came to the dermatologic clinic in December 1942, with palm-sized inflammatory patches covered with silvery scales on the trunk, hips, elbows, legs and scalp and was treated for psoriasis for a year. Occasionally blisters appeared which were thought to be caused by arsenic.

In January 1944, he was admitted to the medical ward with a septic temperature which at times reached 105 F. He was given a course of sulfadiazine therapy, and gradually the fever subsided, although he has never been long without a daily rise of temperature. Large bullae appeared on his skin, especially his arms, trunk and legs. The head was not involved. The patches resembling psoriasis gradually disappeared, and pigmentation, scarring and vesicular lesions predominated. Itching became more severe as time went on. There have never been any lesions of the mucous membranes.

With the exception of the head, where the outbreak is less apparent, the cutaneous surface is practically covered by hyperpigmentation, scarring, crusts and vesicles or bullae, but there are no lesions of the mucous membranes. In some regions, as on the sides of the hips, the patches once regarded as psoriasis still show faintly.

The Wassermann reaction of the blood was negative. The blood sedimentation rate was 16 mm in one hour. A roentgenogram of the chest was normal. A blood count showed 91 per cent hemoglobin and 7,500,000 erythrocytes, and a differential count showed 68 per cent neutrophils, 1 per cent young forms, 1 per cent eosinophils and 30 per cent lymphocytes.

The patient has been treated with sulfonamide compounds, viosterol and arsenic.

#### DISCUSSION

DR MORRIS MARKOWITZ: Irrespective of the fact that this man may have psoriasis and has received arsenic for that disease, it does not follow that that is an arsenical keratosis. I think that dermatitis herpetiformis is the more likely diagnosis. Itching is severe and the pigmentation is prominent, these are important in the diagnosis of dermatitis herpetiformis. The palms and soles, significantly, show no keratosis.



DR FRED D WEIDMAN I thought it dermatitis herpetiformis. There were certainly some vesicles on his feet tonight. Of course, that leaves the lesions at the base of the spine to be explained. I have seen illustrations of lesions as large as that in descriptions of annular dermatitis herpetiformis.

DR ISADORE ZUGERMAN Do you use sulfapyridine?

DR EDWARD F CORSON Before we saw him in the ward he was given sulfadiazine, when he had a considerable elevation of temperature. That lowered the temperature somewhat, but it has never settled down to normal.

DR J M SCHILDKRAUT, Trenton, N J I have seen dermatitis herpetiformis clear with sulfadiazine.

DR MORRIS MARKOWITZ As I have mentioned from time to time in discussing dermatitis herpetiformis, histidine is an important drug for patients with resistant disease. One should give 5 cc of a 4 per cent solution intramuscularly every forty-eight hours.

#### Bromoderma Presented by DR JOHN F WILSON

C G, a white infant aged 7 months, presents an eruption consisting of pea to lima bean-sized firm papulopustules with somewhat fissured opalescent tops. Some of them are elevated 2 to 3 mm. Incision frees little secretion and is accompanied with bleeding. Some are lightly crusted and are best shown on the cheeks and the outer surfaces of the legs. Where adhesive tape was used to hold the biopsy dressing the prompt appearance of similar lesions was noted. The child had been healthy except for a cold (bronchitis?) several weeks ago. The outbreak began rather abruptly about Feb 1, 1944, and the child was brought to the dermatologic clinic on Feb 15, 1944, on account of the second outbreak beginning on the face and legs. The child is breast fed. At first the mother insisted that the baby had taken no medicine, but on March 14 she brought a copy of a prescription of a cough mixture containing 10 grains (0.65 Gm) of sodium bromide to the ounce (30 cc). Three 3 ounce bottles had been taken in seven to ten days each. A routine urinalysis gave normal values. Efforts to obtain sufficient urine to examine for bromides were unsuccessful. A biopsy specimen is on exhibition.

#### DISCUSSION

DR CARMEN C THOMAS Was the serum bromide level determined for this baby?

DR JOHN F WILSON No. Urine was collected for a test for bromide, but, unfortunately, it was discarded and we did not have time to collect another one before the meeting.

DR FRED D WEIDMAN The biopsy specimen was compatible with the diagnosis of bromoderma, but it was by no means typical.

DR ARTHUR G PRATT, Camden, N J We have clinical proof of bromoderma in the fact that the child did not make any progress until we found that it was taking the bromide and that there was remarkable improvement when it was stopped.

#### Juvenile Xanthomatosis Presented by DR J M SCHILDKRAUT, Trenton, N J

M A, a white girl aged 6 years, presents yellow tumor masses on both elbows and knees, bordered by groups of yellow nodules. Lesions are also present at the tip of the spine, on the first and second webs of

the left hand, on the first web of the right hand and on the anterior surface of the right ankle. A new lesion has recently appeared on the left arm. In August 1942, a tumor mass was removed from the right knee. Now there is a crop of new yellow nodules on either side of the scar. The blood cholesterol level was 395 mg per hundred cubic centimeters. The child has been given a low fat diet and thyroid extract, without apparent change.

#### DISCUSSION

DR J M SCHILDKRAUT, Trenton, N J Apparently it is useless to operate, because new nodules have developed along the scar.

DR THOMAS BUTTERWORTH, Reading, Pa I think that the results would be improved with a low fat, high carbohydrate diet plus insulin. I had a patient who was epileptic whose family physician gave him a ketogenic diet and thereafter a severe xanthoma tuberosum developed. After he had been given a low fat, high carbohydrate diet with 10 units of insulin daily, his eruption cleared after about fifteen months, his epilepsy being controlled during that time by diphenylhydantoin sodium. He had one injection daily of 10 units of ordinary insulin.

DR MORRIS MARKOWITZ A patient under my observation has taken 5 units of protamine insulin in the morning and 5 units in the afternoon for several months and has improved about 50 per cent in that time.

#### A Case for Diagnosis (Tuberculosis, Sycosis Barbae?) Presented by COMMANDER H E TWINING

T D, a white man aged 56, presents on the chin, beginning at the angles of the mouth and involving practically the entire chin, a sharply demarcated, erythematous, slightly papillomatous lesion slightly elevated above the normal cutaneous level and partially covered by crust. The same type of lesion is present on the middle of the upper lip. There is mild blepharitis, and there are a few scaly lesions in the left ear. The patient has always enjoyed good health but has lost about 50 pounds (22.7 Kg) in weight in the last few years. His skin was normal until twenty-two months ago, when a small lesion developed on his chin. Since then it has gradually increased in size. About five months later, or seventeen months ago, the same type of lesion appeared on the upper lip, and it has slowly increased in size. The patient is a medium-boned man, weighing about 178 pounds (80.7 Kg). His general physical examination revealed normal conditions.

Complete blood counts and results of a urinalysis were normal. Repeated Kahn tests elicited negative reactions. No fungi were isolated from scrapings. The Mantoux test was negative. A nasal smear was negative for leprosy. A roentgenogram of the chest was normal. A biopsy slide is on view.

Topical treatment, in the form of bland ointments, compresses and shake lotions, has been applied. A course of bismuth therapy and six intravenous injections of oxophenarsine hydrochloride (mapharsen) were given.

#### DISCUSSION

DR FRED D WEIDMAN On clinical examination I thought that this was an unusual sycosis vulgaris, but when I saw the section I did not note the leukocytic infiltration that should be present. The follicles were dilated and hyperkeratotic. Because of the lesion in the ear, I think that this may turn out to be lupus.

erythematosus Unfortunately, the section had been cut parallel to the surface of the skin, so that I could not evaluate conditions deeper in the corium, but I should like to see the paraffin block cut the other way, so that the deeper parts of the corium are cut correctly I should be willing to make the diagnosis of lupus erythematosus profundus

DR H E TWINING I think that there has been a slow progression We have checked carefully as far as laboratory work is concerned and have not been able to find anything that might help in the diagnosis With bismuth I think there has been a slight improvement He has a history of a penile lesion, which may have been chancroid

DR THOMAS BUTTERWORTH, Reading, Pa I think that the presence of blepharitis suggests a coccogenous sycosis I do not think the manifestations of the eye tonight would pass for lupus erythematosus Has any attempt been made to epilate the patient?

DR H E TWINING No

#### Chronic Blepharitis (Cause, Therapy?) Presented by COMMANDER H E TWINING

E M, a white woman aged 29 years, rather thin and not well developed, has had a chronic inflammation of the lower lids for the past twenty-two years It extends about 0.5 to 0.75 cm onto the cutaneous surface, is sharply demarcated and is often covered by a thin, adherent scale Many of the cilia are missing She has had gastrointestinal symptoms for the past six to eight years She had the usual childhood diseases, including measles and diphtheria A roentgenogram of the intestinal tract was normal and a normally functioning gallbladder was found All cutaneous tests for allergy produced negative reactions Several complete blood counts were normal The urine was normal The Kahn reaction of the blood was negative The patient has been given ointments locally, eye washes, massive vitamin therapy, gold sodium thiosulfate and mild roentgen ray treatment

#### DISCUSSION

DR J M SCHILDKRAUT, Trenton, N J I suggest the diagnosis of lupus erythematosus This lesion is chronic and scaly, it looks atrophic, and the inside of the lids does not look quite as inflammatory as in blepharitis, but there is the infiltration of blood vessels one sees in lupus erythematosus

DR H E TWINING That was my first impression, too, and on that assumption I gave her fifteen injections of bismuth and gold sodium thiosulfate and finally, when no improvement occurred, she was given some fractional doses of roentgen rays, which did not produce an exacerbation but rather caused improvement She looks better tonight than she has for some time She has the definite scaling, there has been only one area involved, and she feels that the eruption followed an attack of measles or diphtheria at the age of 7 or 8 years

DR ISADORE ZUGERMAN I had a case similar to this in which the eruption lasted about three years The condition turned out eventually to be due to allergic causes The patient was sensitive to a fluorescent light in his office When the light was removed he recovered I believe that the use of dark glasses would help in this case

DR FRANK C KNOWLES I believe it is a case of seborrheic dermatitis of the scalp

## METROPOLITAN DERMATOLOGICAL SOCIETY

ROYAL M MONTGOMERY, M D, *President*

JAMES LOWRY MILLER, M D, *Secretary*

*April 17, 1944*

#### A Case for Diagnosis (Verruca Plana, Lichen Planus?) Presented by DR MAURICE J COSTELLO

P B, a woman aged 24, presents a generalized eruption, without lesions of the mucous membranes, which involves the sides of the neck, arms, forearms, the inner aspects of the thighs and anterior aspects of the legs The eruption is of six months' duration The individual lesions are sharply demarcated, flattened, slightly elevated, umbilicated violaceous and salmon-colored papules, from pinhead to matchhead size

Therapy has consisted of subfractional doses of low voltage roentgen rays, intramuscular injections of bismuth subsalicylate and liver extract

#### DISCUSSION

DR LESLIE P BARKER Clinically, this case suggests one of lichen planus, although some of the lesions on the leg have the characteristics of epidermodysplasia verruciformis

DR J LOWRY MILLER I agree with the diagnosis of lichen planus

DR THOMAS N GRAHAM If I had to decide between lichen planus and verruca plana juvenilis in this case, I should make a diagnosis of the latter I find no lesions typical of lichen planus, but many of the lesions show all the characteristic features of verruca plana juvenilis I believe that biopsies should be performed of sections from several lesions in order definitely to establish a diagnosis

DR ROYAL M MONTGOMERY This case resembles one of verruca plana more than one of lichen planus Some of the lesions on the legs are typical flat warts Considering also the history of lesions on the neck which disappear quickly, I favor the diagnosis of verruca plana

DR LAIRD S VAN DYCK In the first place there is considerable itching, a point strongly in favor of lichen planus I saw one glistening papule on the right forearm There is a history of a recent death in the family which one frequently finds in cases of lichen planus There are some lesions, especially the ones on the legs which are characteristic of verruca plana I think that in this case I should make two diagnoses lichen planus and verruca plana

DR MAURICE J COSTELLO The dermatologists who saw this young woman before I did was treating her for "warts" The lesions on the forearms are shiny, flat, umbilicated and polygonal They are skin color, with a yellowish rather than a violaceous tone Severe pruritus is a constant feature Interspersed with them are a number of lesions that appear to be verruca plana Similar lesions on the neck disappeared with the application of roentgen rays

#### Lupus Vulgaris Presented by DR ROYAL M MONTGOMERY

M M, a man aged 49, has had the present eruption for over twenty years The plaque on the neck followed an abscess dating from the time the patient was

a boy Twenty years ago, following a scratch which the patient received in World War I, the involved area gradually enlarged until it attained its present size

At present on the right anterior cervical region there is a plaque 4 by  $1\frac{1}{2}$  inches (10 by 38 cm), which is dull red and indurated and scaly Below this there is a U-shaped area, about 4 inches (10 cm) by  $\frac{1}{4}$  to  $\frac{1}{2}$  inch (0.6 to 1.3 cm) Scarring is present in the center Recently it has extended over the larynx for  $\frac{1}{4}$  to  $\frac{3}{8}$  inch (0.6 to 1 cm)

He was treated with ultraviolet rays for one year, with improvement of the eruption Later it failed to respond Three days ago a small area of the lower part of the plaque was destroyed by electrosurgery

The pathologic diagnosis is lupus vulgaris

#### DISCUSSION

DR JOSEPH C AMERSBACH I believe that I am correct in thinking that the patient has begun treatment by electrodesiccation I believe that this treatment is adequate

DR THOMAS N GRAHAM Apparently ultraviolet irradiation is no longer effective in this case I believe that a satisfactory result can be obtained with electrodesiccation

DR J LOWRY MILLER The best treatment in this case would probably be complete destruction with the electric cutting current, applied through a wire loop The entire operation should be done in one sitting, the wound should be dressed with wide mesh petrolatum gauze and allowed to granulate The resulting scar would be remarkably pliable Plastic surgical procedures are contraindicated because of the size of the lesion

I have a patient now with a similar but more extensive lesion who refused hospitalization As a second best treatment, solid carbon dioxide has been applied to a portion of the lesion about every three weeks This length of time is generally required to heal the ulceration produced during each treatment Cure has not been obtained because of recurrence in the treated area This is the objection to any method short of complete destruction at one sitting

DR MAURICE J COSTELLO I believe that the diseased area should be excised widely by a plastic surgeon, because there are always satellite lesions not clinically visible beyond the borders of the patch The affected area should then be covered with a skin graft I do not see why that cannot be done in this location Injections of tuberculin in gradually increased doses over a long period should be tried Patients have been treated with a degree of success with tuberculin-containing ointment rubbed on the patch of lupus vulgaris Fractional electrodesiccation will take a long time A history of another form of cutaneous tuberculosis is not infrequent in cases of lupus vulgaris of the clavicular region Tuberculous lymphadenitis may eventuate in scrofuloderma or lupus vulgaris at the site of the disease

DR ROYAL M MONTGOMERY A clinic patient who had lupus vulgaris had a plastic repair on the entire left side of the face I did not see her before the operation, but I saw photographs of her Immediately afterward the results were excellent Later lupus vulgaris nodules that were extensive developed in the plastic repair Therapy in the case presented here is a problem Dr Miller suggested extensive electrosurgery That and plastic surgery are the two courses to follow

### Lupus Erythematosus, Pityriasis-Rosea-Like Dermatitis Following Therapy with a Gold Salt Presented by DR LAIRD S VAN DYCK

F J F, a ship's plumber aged 39, has had a reddish patch in front of his left ear for the past six years At the age of 10 years he had an operation for enlarged lymph nodes on the right side of his neck

In 1939, he received twelve injections of bismuth subsalicylate intramuscularly and sixteen injections of gold sodium thiosulfate intravenously, which cleared the patch on his left cheek In May 1942 he went to East Africa, where he was exposed to bright sunlight The lesion on his cheek recurred and became enlarged and inflamed He received many injections of a gold salt in 1943, with improvement of the lupus erythematosus In December 1943 a lesion resembling ringworm appeared on his shoulder A culture of material from the lesion examined at the United States Marine Hospital was positive for fungi In March 1944 another culture prepared at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital was negative During the past few weeks new lesions have appeared on the trunk, which resemble pityriasis rosea Injections of a gold preparation have been discontinued

In the left preauricular region is a sharply outlined erythematous and scaly patch showing telangiectasia and atrophy Scattered over the trunk are oval and circinate erythematous and scaly patches, some of which have been present for four months and others, for two or three weeks

The Wassermann reaction of the blood was normal

#### DISCUSSION

DR ROYAL M MONTGOMERY I believe that the eruption on the body is due to therapy with a gold salt and to secondary eczematization I feel that there might have been a mistake in the first examination for tinea I am inclined to discount that examination and accept the results of the one made at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, which was negative The configuration of the patches does not point to a fungous infection Roentgen therapy has improved the eczematization

DR JOSEPH C AMERSBACH The eruption is probably due to the gold preparation I had a patient with a similar eruption following therapy with a gold salt

DR THOMAS N GRAHAM I agree with Dr Montgomery that this eruption is probably due to the gold preparation The pigmentation of the lesions strongly suggests this diagnosis I think that this eruption does not resemble tinea circinata, because of the pigmentation as well as the absence of normal-looking skin in the centers of the patches

DR J LOWRY MILLER I agree with the diagnosis of dermatitis medicamentosa, because of the history and the type of lesion present In a fair number of cases observed at the Vanderbilt Clinic the eruption has resulted from gold sodium thiosulfate used in the treatment of arthritis This type of lesion is not uncommon in such cases Soreness of the tongue, particularly at the onset of the disease, is common I should like to ask if that symptom has been noted in this case

DR MAURICE J COSTELLO I think that this eruption is a dermatitis medicamentosa due to the injection of gold salts I have seen a fair number of patients with lupus erythematosus who have had tuberculous lymph-

adenitis or who gave a family history of pulmonary tuberculosis. Patients with lupus erythematosus should be examined for tuberculosis with this in mind.

DR LAIRD S VAN DYCK This patient returned from Africa with a circinate lesion on his back and several smaller ones on his chest. They had been diagnosed as *tinea circinata*, and scrapings examined at a hospital laboratory were reported as being positive for fungi. I prescribed fungicidal remedies, which only aggravated the eruption. Soothing applications and roentgen therapy brought improvement. When treatment of his lupus erythematosus with injections of 50 mg of gold sodium thiosulfate was resumed, new lesions, resembling pityriasis rosea, appeared on his abdomen. Injections of the gold salt have been discontinued.

## CHICAGO DERMATOLOGICAL SOCIETY

L M WIEDER, M D, *President*

MARCUS R CARO, M D, *Secretary*

*April 19, 1944*

### Hodgkin's Disease with Pruritus Presented (by invitation) by DR MARTHE ERDOS-BROWN

F W, a white woman aged 37, complains of an intense generalized itching of five months' duration. Two years ago, at the New York Memorial Hospital, a diagnosis of Hodgkin's disease was made, based on biopsy of a cervical node. The patient had twenty to thirty roentgen ray treatments in New York and Chicago without any subjective improvement in the itching. Since the beginning of her illness she has lost about 30 pounds (13.6 Kg).

On both legs, the back and the buttocks there are numerous papules irregularly distributed. They are red and slightly scaly and are somewhat below the level of the skin. Once healed, they leave depigmented areas. The face is free of lesions. Local treatment has had little effect, and the eruption is highly resistant to internal medications, although the patient feels that calcium gluconate by mouth has helped her a little.

The hematologic examination on Feb 3, 1944 showed 3,530,000 erythrocytes and 25,050 leukocytes, with 75 per cent polymorphonuclear leukocytes, 4 per cent lymphocytes and 7 per cent monocytes.

The liver and spleen are not palpable.

#### DISCUSSION

DR ARTHUR C CURTIS, Ann Arbor, Mich (by invitation) I agree with the diagnosis in view of the type of lesion. There are numerous lesions that have apparently healed without scarring. The likelihood is that the eruption is a lymphoblastoma of the Hodgkin type.

DR MAURICE OPPENHEIM (by invitation) The case is certainly one of Hodgkin's disease because the lesions are advancing to tumors and because they are extending to other parts of the body. I suggest that a tuberculin test be given.

DR MARTHE ERDOS-BROWN (by invitation) I shall follow Dr Oppenheim's suggestion and give either a tuberculin or a von Pirquet test. I presented the case with a question in my mind as to whether the lesions were an independent disease of the skin or a manifestation of Hodgkin's disease.

### A Case for Diagnosis (Congenital Ectodermal Defect, Moniliasis?) Presented by Dr THEODORE CORNBLEET and (by invitation) DR D COHEN and DR H C SCHORR

E L, a woman aged 20, has a disorder of her nails, which she thinks has been present since birth. Eight finger nails are involved and are now present as mere stumps, thickened, opaque and supported by debris. The nail beds are not keratotic. Two of the finger nails are apparently normal. One of the latter had been equally involved with the other eight, but the patient claims that it grew to its present appearance after a surgical avulsion. The toe nails are similarly affected. There is a scaling erythema at the webs of the fingers. The commissures of the lips show a scaling maceration. The tongue is vividly red, smooth and atrophic. The scalp is bald.

The patient is blind. She was told that she had *interstitial keratitis*. She does not perspire freely but is not uncomfortable in the summer, although her palms and soles show free sweating when she becomes nervous.

The serologic reaction for syphilis was negative, and scrapings from the nails had enormous numbers of yeastlike organisms but no hyphae.

#### DISCUSSION

DR J H MITCHELL I should like to ask whether the cultures were positive. In looking at the nails I noticed that the characteristic paronychia is not present. Clinically, the nails resemble nails affected with ordinary ringworm more than ones with moniliasis.

DR C W FINNERUD I should like to know how early fungi were found. The lesions at the angles of the mouth are compatible with moniliasis, but the patient has unusual manifestations of the nails in the absence of paronychia.

DR THEODORE CORNBLEET The scrapings from the nails showed an enormous number of yeastlike organisms. There were no hyphae present. I do not know whether the organisms that were present are actually causing the disturbances of the nails. I am not making a diagnosis of moniliasis, though the lesions of the lips are somewhat suggestive. I know of no reference in the literature which states that any particular work has been done to show that moniliasis of the nails necessarily produces paronychial changes or that such changes must be present before the nail is involved. It is possible that such a thing happens in each case.

I am more interested in the vestigial changes which fit in with an ectodermal defect. The patient stated that the changes in the eye were diagnosed as syphilis, but Jadassohn, in a description of cases similar to that of the patient's diagnosed them simply as "dyskeratosis of the cornea." There are other changes present in this case which somewhat suggest dyskeratosis of the skin. Jadassohn was of the belief that in such a case there are numerous changes present in the skin which are somewhat related. No two patients show the same picture but all such pictures are classed in the group of general ectodermal defects. It is from that standpoint that the case interests me.

### Lupus Vulgaris Presented by DR A B HENNINGSEN (by invitation)

This 45 year old white woman was first seen at the University of Chicago Clinics yesterday, April 18, 1944. She first noticed a lesion on her right temple thirty-

three years ago Thirteen years ago the lesion began to spread Three years ago the patient received injections of a gold preparation twice a week for one year, without results Her general health has always been good

The extended, sharply limited infiltrated lesion, on the right side of the face, scalp and neck, shows all the characteristic features of lupus vulgaris Lupus verrucosus, lupus tumidus and the hypertrophic-ulcerative form are all represented in this lesion

The fluoroscopic examination showed no pulmonary tuberculosis The intradermal tuberculin test with old tuberculin, diluted 1:10,000, elicited a positive reaction The Kahn reaction of the serum was negative

#### DISCUSSION

DR H E MICHELSON, Minneapolis To me, unfortunately, lupus vulgaris is a fascinating disease Although the diagnosis is accepted rather readily, I wonder whether one takes the pains to study the cases as thoroughly as one might This woman presents changes which to me are striking It is known that the pathologic changes in lupus vulgaris have a tendency to go deep The differential pathologic diagnosis depends on whether lymphatic stasis or scarring is present In this woman, in spite of the location of the lesion, there is no induration of the eyelids, no narrowing of the palpebral canal and no trouble with the ear She carries on her work in a factory, and the disease has not affected her, either physically or psychologically

As to therapy, I do not know what to suggest She has had the lesion for thirty-three years, and I believe that she will live her life just as well if she is let alone

DR FRANCIS W LYNCH, St Paul As Dr Michelson said, there is no evidence of scarring From its appearance, the eruption is superficial Although the patient is unable to close her eyes completely, there is no facial paralysis on the right side

DR LOUIS A BRUNSTING, Rochester, Minn I should like to call attention to the ulceration in the center It is known that occasionally lupus vulgaris degenerates into a malignant process This point should be looked into I do not know how the case should be managed from the standpoint of treatment

DR S ROTHMAN (by invitation) I feel that clinically the lesion is not malignant, though I did suspect it As to therapy, I should first remove the secondary crusts or scales I believe that I should not start with pyrogallol, as has been suggested

DR A B HENNINGSSEN (by invitation) It is rather interesting that in spite of the lesion on the face, this patient has been married twice and has two adopted children

**Adenoma Sebaceum (Pringle?)** Presented (by invitation) by DR S ROTHMAN and DR A L SHAPIRO

D W, a schoolgirl aged 15, was first seen in the Dermatology Clinic of the University of Chicago on June 30, 1937, when she was 8 years old At that time she presented an eruption of six years' duration on the nose, cheeks, chin and lips, consisting of small discrete reddish papules The clinical diagnosis was Pringle type of adenoma sebaceum The patient also presented a verrucous papilloma (verified by biopsy) of the right second toe The facial lesions were treated with solid carbon dioxide with good cosmetic results, but the patient objected to the treatment and stopped coming to the clinic The case was reported by H W

Woolhandler and S W Becker in their paper "Adenoma of Sebaceous Glands" (ARCH DERMAT & SYPH 45:743 [April] 1942)

On March 20, 1944, about five and one-half years after her last visit, the patient returned to the clinic and stated that there had been an increase in the number of lesions in the nasolabial folds She now presents multiple papules, flesh-colored, brown and brownish red, pinpoint to pinhead sized, mainly in the central region of the face and chin as previously described She is mentally alert, and she is doing well at school

#### DISCUSSION

DR S W BECKER I treated this girl many years ago, and one can see several free areas on the cheeks and nose where solid carbon dioxide was used The result evidently has been permanent in the areas which were treated

DR M H EBERT It is pretty generally recognized that adenoma sebaceum is only a manifestation of tuberous sclerosis It is rather extraordinary that this girl has no other manifestations She has no tumors of any type, and she stated that she has no nevi

I am pleased to see the results of Dr Becker's treatment with solid carbon dioxide In the outpatient department there is a boy of low grade mentality with many sebaceous cysts, who has been shown before this Society He is being treated with solid carbon dioxide, largely for the psychic effect, to make him feel that he is having something done for his disease

DR OTTO FOERSTER, Milwaukee The lesions in this patient are small, some almost miliary, which, I think, is unusual The lesions were considerably larger in most of the cases that I have encountered In 1913 4 cases were presented in which the patients were all from the same family, and in only 1 was there tuberous sclerosis

DR S ROTHMAN (by invitation) The lesions are too small for tuberous sclerosis In all the cases that I have encountered previously there were larger lesions, and in all there was more or less telangiectasia present Dr Becker, in his publication, emphasized the cases in which episcleritis can be found It is interesting that the patient had a papilloma on one of the toes Dr Shapiro found in the literature 3 or 4 cases of tuberous sclerosis with papilloma on the toes

**A Case for Diagnosis (Lichen Syphiliticus [Extragenital Infection], Lichen Scrofulosorum?)**

Presented by DR S W BECKER and (by invitation) DR E A STRAKOSCH

B S, a Negro girl aged 8, was referred to the Chicago Intensive Treatment Center on April 5, 1944, because of a cutaneous eruption and a Kahn titer in her blood serum of 280 units She gave a questionable history of having had a sore on the dorsum of the left foot, which appeared approximately five to eight weeks before admission Subsequently, two ulcers appeared on the upper third of the left thigh, which broke down and discharged pus Four to five weeks prior to admission a generalized cutaneous eruption had been noted

On examination there was an indurated plaque in the center of the dorsum of the left foot and two indurated, partly healed ulcers on the anteromedial aspect of the upper third of the left thigh, which were discharging pus On the trunk, neck, arms and legs was a lichenoid eruption, which was grouped in annular or oval arrangement, with some scaling in the center No genital or mucosal lesions were found

A roentgenogram of the chest showed a questionable primary complex in the lung. Repeated examinations of scrapings and pus from the ulcers on the thigh revealed no tubercle bacilli. The Mantoux test, with a 1 to 10,000 dilution of tuberculin on the right arm, elicited a strongly positive reaction.

The quantitative Kahn titer of the blood serum was as follows: 280 units on April 1, 160 units on April 4, and 80 units on April 6.

No treatment has been administered.

#### DISCUSSION

DR UDO J. WILE, Ann Arbor, Mich. It seems to me that the differential diagnosis between lichen scrofulosus and lichenoid syphilid is sometimes quite impossible unless one has associated observations of the two diseases. I feel that this child has lichen scrofulosus, even though the appearance of this lesion is more difficult to differentiate in a Negro patient than in a white one.

DR E. A. OLIVER. For the same reasons Dr. Wile has given and because of the pathologic changes in the chest, I feel that this is lichen scrofulosus rather than a lichenoid syphilid.

DR H. E. MICHILSON, Minneapolis. The case is difficult to analyze because one cannot call on one's memory to help. I have not seen anything just like this eruption, so I have to make a diagnosis by analysis. I have never seen a syphilitic eruption acquired in a child so young. If it were syphilis, I should expect other symptoms. This eruption is more like sarcoid or tuberculosis in the Negro. I should be more apt to think that it is lichen scrofulosus, as there are enlarged lymph nodes and other signs that point in that direction.

DR MAURICE OPPENHEIM (by invitation). I have observed cases of lichen scrofulosus, but I am really in doubt as to whether this is one of lichen scrofulosus or syphilid.

DR S. ROTHMAN (by invitation). In this case there are no grouped follicular lesions such as are present in lichen syphiliticus. I accept Dr. Michelson's statement that the lesions have a sarcoid-like structure.

DR M. R. CARO. I had occasion to examine a section from this patient taken about two weeks ago. At that time the changes were vascular and perivascular, and there was thickening of the vascular wall. The infiltrate consisted largely of lymphocytes. I made a diagnosis of possible syphilis. The biopsy specimen from the foot has a different picture and, as Dr. Michelson says, fits in with sarcoid or the type of tuberculosis seen in the Negro.

DR UDO J. WILE. I am sure that I have seen this eruption in children. My attention has been called to it by pediatricians in cases of generalized tuberculosis with accentuation of the grouped lesions. I think that it is not as rare as would seem to be indicated by the discussion. Those who have to do with tuberculosis in children see more of it than dermatologists do.

DR S. W. BECKER. This child presented some difficulties. There was another patient the same day, a middle-aged Negro man, who had grouped follicular lesions which to me seemed to be identical with the child's, but in his case they covered the entire body, even the scalp. My initial diagnosis was lichen scrofulosus, for the reason that this child gave a history of having had a sore on the foot. After a few weeks these ulcerative lesions on the left thigh appeared in the region of the femoral lymph nodes, though I had felt

no enlargement of the lymph nodes. A few weeks later the generalized eruption developed. I think that it is probably lichen scrofulosus. The patient had a high titer in the original Kahn reaction, and that titer has gone down too rapidly to represent a reaction to syphilis. It may be a nonspecific reaction. If the eruption is a primary inoculation tuberculosis, it is unusual, because this sarcoid structure is not the ordinary picture that is seen. The history was suggestive of an inoculation tuberculosis with lymphadenopathy and later this generalized eruption.

#### Generalized Progressive Scleroderma with Involvement of the Glottis and Esophagus Presented (by invitation) by DR S. ROTHMAN and DR Z. FELSHER

V. F., a white woman aged 43, was well until November 1941, when she began to have pain in the fingers, which rapidly spread to the lower extremities, shoulders and spine. Soon thereafter she noticed easy fatigability and generalized weakness, with widespread and increasing thickening and hardening of the skin. The motion in all joints, especially in those of the hands and fingers, became limited. In June 1942 she began to have difficulty in swallowing food, resulting in regurgitation, especially of solids. This has continued to the present time.

The physical examination reveals an undernourished white woman, chronically ill and unable to get about without aid. The skin is dry, hard and stiff, with large areas of brown pigmentation, especially on the neck, waist, pubes and feet. The fingers are deformed, and motion of the joints is limited. The extremities are wasted. The voice is nasal in quality. The laryngologic examination showed inability of the glottis to close. Esophagoscopy showed no abnormalities, but fluoroscopic examination revealed a characteristic loss of pharyngeal movements and esophageal peristalsis, involving both voluntary and involuntary muscles. The soft palate was involved in the atrophic process. Roentgenograms showed osseous changes characteristic of scleroderma. There was interstitial calcinosis of the soft tissue about the knees.

The laboratory examinations revealed no abnormalities except a mild leukocytosis, with a low grade temperature.

#### DISCUSSION

DR C. W. LAYMON, Minneapolis. If one accepts the view that scleroderma is a process that affects all the structures in the body, then probably the internal structures are involved more frequently than is realized. A few years ago Weissenbach, in the *Bulletin de la Société française de dermatologie et de syphiligraphie*, reported a dozen cases of scleroderma with involvement of the esophagus. He found various changes in the esophagus from leukoplakia to stenosis of the esophagus, and he even found involvement of the stomach.

DR S. ROTHMAN (by invitation). An unusual feature of the case was the blood picture.

#### A Case for Diagnosis (Lupus Erythematosus?) Presented by DR HERBERT RATTNER and DR MAURICE DORNE

Mrs. E. J., a white woman aged 54, states that about one year ago she first noted slight redness, puffiness and itching of the eyelids. Gradually the redness extended to involve the entire face, forehead and neck, at the same time red patches appeared on the fingers. Later the forearms and buttocks became involved. About six months ago she began to suffer from attacks



of diarrhea. She has lost 45 pounds (20.4 Kg) during the past year, has become progressively weaker and in the past few months has noted that the muscles of the neck have been getting weaker.

The examination revealed a rather diffuse erythema of the face, well defined patches on the neck and chest extending beyond the "V," the sacral region, the dorsal surfaces of the hands and the nail folds and symmetric patches on the outer surfaces of the forearms. The patches have a superficial resemblance to sunburn, but in places there appears to be atrophy around the follicles, telangiectasia and a reticulated bronze hyperpigmentation. There are some discrete erythematous lesions on the vermilion borders of the lips and telangiectatic spots on the buccal mucous membranes and hard palate.

High voltage roentgen therapy was applied over the pubic region and on each buttock for a lesion of the rectosigmoid. There is diffuse pigmentation of the skin of the pubic area and a sharply demarcated patch of pigmentation on each buttock. Within each of the latter areas there is a smaller patch with erythema, atrophy and telangiectasia.

The examination of the blood showed hemoglobin content, 51 per cent, erythrocytes, 3,020,000, leukocytes, 5,000, with a differential distribution of 77 per cent polymorphonuclear leukocytes, 1 per cent eosinophils, 1 per cent basophils, 6 per cent lymphocytes and 15 per cent monocytes, anisocytosis 2 plus, poikilocytosis 2 plus, and polychromatophilia 1 plus. The Kahn reaction was negative. Determination of the blood chemistry showed nonprotein nitrogen content 27 mg, total protein 47 mg, albumin 29 mg and globulin 18 mg per hundred cubic centimeters. The basal metabolic rate was plus 15 per cent.

#### DISCUSSION

DR OLIVER S. ORMSBY: I think it is lupus erythematosus.

DR M. H. EBERT: I had an opportunity to see this woman in the ward. There was a rather confusing picture. It seemed from the medical report that there was some stenosis of the rectum, probably due to a tumor, which might have accounted for the diarrhea and loss of weight. On the other hand, she had a low grade fever, with a temperature at times up to 101 F. The lesions on the skin were practically the same as today. On the backs of the hands there were some red plaques. There was some edema at the nail folds and some dilatation of the vessels on the palms. In addition, the patient had peculiar poikiloderma-like changes on the back and on the chest. She had a diffuse erythema of the face. In places there was definite atrophy. She had erosions in the mucous surface of the mouth. In spite of the temperature the leukocyte count was only 4,000. Considering the entire picture, I made a diagnosis of acute disseminated lupus erythematosus, in spite of the fact that the lesions on the back were unusual. I had never seen anything like them. The changes in the section will, I think, bear out that diagnosis. I saw the patient before the sections were made.

DR F. W. LYNCH, St. Paul: There are points that are in agreement with a diagnosis of lupus erythematosus. One is the acute nature of the involvement, another is the sharply outlined eruption on the chest. There are no lesions beyond the costal border. The eruption is not only diffuse but equally separated throughout most of its extent. The histologic sections favor lupus erythematosus, though there is not much follicular dilatation and scaling. There is a definite

involvement of the connective tissue, which I have not seen in lupus erythematosus. The specific stain for elastic tissue showed fragmentation completely down to the connective tissue.

DR EDWARD A. OLIVER: One has to consider the possibility that this woman will eventually have poikiloderma. The history of the eruption beginning on the face, the involvement of the eyelids and auricles and the character of the eruption are similar to the features of Jacobi's original case. When Jacobi's case was originally presented, there was a difference of opinion as to what the disease was. There were signs and symptoms of lupus erythematosus, and that diagnosis was considered by some of the men who differed with his diagnosis of poikiloderma. I believe that poikiloderma cannot be ruled out and that this woman will have to be watched.

DR LOUIS A. BRUNSTING, Rochester, Minn.: In older people lupus erythematosus has a milder course. The thing that struck me was the degree of myositis. The patient has telangiectasia of the face but not enough changes to be suggestive of lupus erythematosus, but, as Dr. Oliver said, there are enough changes to make one think of poikiloderma. The striking feature was the lichenoid plaques on the ankles and on the elbows and knees. It is always difficult to differentiate between subacute and acute disseminated lupus erythematosus. I suggest that an examination be made for creatinuria.

DR THEODORE CORNBLEET: This woman has a low proteinemia, though the albumin-globulin ratio is normal. That picture is one which is found repeatedly in lupus erythematosus disseminatus.

DR LOUIS A. BRUNSTING: That will occur in many wasting diseases if the patient is not properly nourished.

DR MAURICE OPPENHEIM (by invitation): It is striking to see the weakness of the muscles. I suggest, first, an examination for collagen and then biopsy of a specimen from the muscle.

DR S. J. ZAKON: The patient told me that she starved herself for a year and a half because of the diarrhea, living only on liquids. That explains some of the atrophy of the muscles and some of the changes in the blood chemistry.

DR HERBERT RATTNER: I am at a loss with regard to classifying this case. There is much to suggest lupus erythematosus, yet the poikiloderma-like changes dominate the clinical picture. I attributed the profound weakness of the patient to the presence of carcinoma of the sigmoid with resultant diarrhea and lack of appetite, it was not until Dr. Brunsting's suggestion was made that I gave any thought to the probability that this is a case of dermatomyositis. All the symptoms fit in well with that diagnosis, and further investigations along that line will be made.

NOTE—Biopsy of the muscle showed changes typical of dermatomyositis.

**A Case for Diagnosis (Tuberculid?)** Presented by DR M. H. EBERT and (by invitation) DR M. OTSUKA

R. M., a white man aged 40, presents lesions on the face of eight years' duration and on the cornea of both eyes of seven years' duration. A poorly defined erythematous band extends from the level of the zygoma to the jaw on either cheek. The chin and the right side of the forehead are similarly affected. In these areas are numerous pinhead-sized follicular papules. No color remains under diascopic pressure. The lobes of the ears are bright red and slightly edematous.



The ophthalmologic department of Cook County Hospital reports that in the left eye there is a 3 plus ciliary congestion in the temporal sector. A pterygium-like conjunctival infiltration extends up to the pupillary area. At the apex there is a yellowish white plaque. In the right eye there is a triangular leukoma on the nasal side of the cornea. The clinical impression is that of rosacea keratitis. There was a strong reaction to a 1:100,000 dilution of Koch's old tuberculin injected intradermally. The leukocyte count was 10,400, with a normal differential count. The hemoglobin content was 92 per cent, and there were 5,200,000 erythrocytes. The blood chemistry was normal. The roentgenogram of the chest was interpreted as showing increased fibrotic markings throughout both lungs, with some evidence of an old infiltrative process involving the left infraclavicular region. The picture was compatible with an old fibrotic area of tuberculosis.

#### DISCUSSION

DR JOHN F. MADDEN, St. Paul: Because of the localization of the process, I thought of a sensitization to light, though apparently the eruption was not intensified by exposure to sunshine. The lesions themselves are not such as one sees in lupus erythematosus. Some of them are pustular. There are certainly separate lesions on the nose and forehead.

DR C. W. FINNRLD: I did not see the section, but I thought, without too much imagination that there was some rather characteristic color remaining after diascopic pressure. I rather felt that while it is not a classic rosacea form of tuberculid it might well be a manifestation of tuberculid in some form or other.

DR M. J. REUTER, Milwaukee: The eruption had many characteristics of rosacea, particularly the involvement of the midline of the face. I thought that there were definite pustular elements present. I favor a diagnosis of rosacea. If it is rosacea, the eruption may be cleared rapidly by the use of sulfosalicylic acid paste.

DR H. E. MICHELSON, Minneapolis: Dr. Winer and I have been interested in the problem of whether rosacea is tuberculous or whether there is such a disease as a rosacea-like tuberculid. The answer will come, I think, if one studies rosacea. There is no entity that has as many variations as rosacea. I think that this man has the *en plaque* type of rosacea. I do not believe that the therapeutic test, as suggested by Dr. Reuter, is valuable in rosacea. There are many cases of rosacea in which treatment of every known kind has been tried, but without result. I believe that one cannot say that because the disease does not respond it is something else.

DR M. H. EBERT: This patient was referred to the outpatient dermatologic department by the ophthalmologic department. They were particularly interested in the case because of the unusual changes in the cornea of both eyes. They described a leukoma in the right cornea with some pterygium-like lesion. In one eye there is a ciliary congestion. When I examined the patient my first thought was rosacea with ocular changes. I have seen rosacea with congestion of the conjunctiva, such as this man has. The leukoma might be a sequel to an ulceration of the cornea. My next thought was a Lewandowsky type of tuberculosis, and that is why a biopsy specimen was taken. The first specimen was not satisfactory. The second one, taken two days ago, revealed the structure rather clearly. I am still somewhat in doubt about the diagnosis, though I still favor rosacea. I agree with Dr. Michelson that the term "rosacea" covers a wide range of clinical

manifestations, but I have personally never seen this particular type of rosacea with this peculiar bandlike arrangement, beginning at the level of the zygoma and extending down each cheek. I also had the rather far-fetched idea that this might be some manifestation of lymphoblastoma, and for that reason I had a blood count made. There were no significant changes, but I thought that the patient should be observed with that in mind. The ophthalmologic department is anxious that the diagnosis of the cutaneous eruption be reported, and in the circumstances I shall say rosacea.

#### Systemic Blastomycosis Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS

S. B., an Italian detense worker aged 59, presents an eruption of three weeks' duration, which is composed of variably sized nodules involving the face, body and extremities. These nodules are sharply defined, with sloping edges, and are crust covered, with evidence of miliar abscesses in the vicinity of the edges. The examination of the pus expressed from these lesions reveals the budding organism of Blastomyces.

The patient states that six weeks ago bronchitis developed. One week after the onset he consulted a doctor, who hospitalized him for six days. He had improved to the extent that he was discharged as cured. About one week after leaving the hospital the first lesion appeared on the chin, and others soon followed. The examination of the early lesions shows a deep nodular infiltrate, which gradually becomes larger, involving the overlying skin, and breaks down with classic lesions as seen today. The patient was seen for the first time last night.

#### DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I wonder whether Dr. Omens would consider nodular bromoderma. As I understand, the lesions were present for only three weeks, a rather short time for blastomycosis. The lesions are inflammatory. I think that the organisms may be secondary invaders.

DR. J. H. MITCHELL: My impression is the same as Dr. Wile's. If blastomycetes were present in the section I did not find them, though the time devoted to studying the section was short.

DR. EDWARD A. OLIVER: I should like to ask if there are symptoms of systemic blastomycosis and any pulmonary symptoms. If the eruption is a systemic blastomycosis, would not the name of this disease be disseminated lesions of blastomycosis rather than systemic blastomycosis?

DR. M. H. EBERT: I thought that I saw a budding double contour organism. I think that Dr. Wile's point is excellent. It is easy to make a diagnosis of blastomycosis when the disease is protracted.

DR. O. S. ORMSBY: The lesions in the skin are not those of cutaneous blastomycosis, they are simply ulcers and crusted lesions occurring on top of deep-seated abscesses. I had the privilege of working up the first case reported of systemic blastomycosis, and that patient had multiple nodules all over the body. The pus obtained on puncture of one of the lesions was loaded with blastomycetes. The lesions today looked like a bromide eruption. I saw no typical subcutaneous abscess, though there was one that was somewhat suggestive. I am rather doubtful about this being a systemic blastomycosis. I have never encountered a case of the acute disease in which the lesions resembled these.

DR M R CARO Blastomycosis is sometimes mistaken for a drug eruption

DR E A OLIVER If this is a blastomycosis, it is not systemic, it is rather a blastomycosis with numerous lesions

DR J H MITCHELL A number of years ago a patient with widely disseminated blastomycotic lesions was presented to the Society. They were typical cutaneous lesions—none of this type at all. He had hundreds of small lesions. I had him under observation in the clinic for a considerable length of time, then he went to New York. When he returned the lesions had grown to enormous size. There was no systemic involvement.

DR DAVID V OMENS I saw this patient for the first time last night, and on examination of the pus I found the budding organism twice. I thought that I should verify this observation, and on the next examination I saw the organism three or four times. I showed the slide to Dr Ebert, and he thought that budding organisms were present. The patient is a healthy Italian who works in a factory, interviewing people who operate machines. He had no occasion to use drugs. He gave a history which was suggestive of bronchitis. He did nothing at all about his symptoms for a week, not getting better, he consulted a physician. When the lesions on the skin developed, the doctor sent a specimen of the serum to a laboratory, where a diagnosis of blastomycosis was made. He then referred the patient to me.

DR UDO J WILE The patient told me that the physician he had during the attack of bronchitis did nothing for him.

DR DAVID V OMENS He was hospitalized for six days and the bronchitis cleared entirely. He could not accumulate enough bromides in that length of time to produce an eruption.

DR UDO J WILE He may be bromide-sensitive. There are cases in which bromoderma developed in a child from one dose of a bromide taken by the mother.

DR DAVID V OMENS He still would not have had the budding organism present.

DR UDO J WILE That is true. We were talking about the size of a dose of bromide that could cause an eruption.

**Lichen Striatus** Presented by DR F E SENEAR and DR M R CARO

R L, a man aged 29, noticed an eruption in the right crural region four months ago. Recently an extension of the eruption has appeared on the lower part of the thigh and the upper part of the leg. There are practically no symptoms. On examination the patient was found to have a band of dermatitis involving the right crural region. This band is about 1 inch (2.5 cm) in width at the top and at the base narrows down to a width of  $\frac{1}{2}$  inch (1.3 cm). It consists of a number of individual and confluent papules, which are bright red, not infiltrated and slightly lichenoid in character. Just above the knee there is a narrow threadlike band about 1 inch in length, while below the knee two similar shorter narrow bands are seen.

Histologic examination of a section from the right thigh showed a thin nonnucleated scale and a continuous granular layer. The epidermis was acanthotic, with irregular widening and fusion of the rete pegs and an intact basal layer. There was slight intercellular edema and in places invasion by a few lympho-

cytes from the corium. There was a moderate degree of edema in the upper part of the corium, and about the superficial blood vessels there were narrow mantles of densely packed lymphocytes, connective tissue cells and histiocytes. These mantles of infiltrate extended more deeply about several blood vessels.

#### DISCUSSION

DR M H EBLERT I have encountered 2 or 3 cases of lichen striatus in the clinic since Dr Senear and Dr Caro called attention to it, and this case resembles them.

DR EDWARD A OLIVER I agree with the diagnosis of lichen striatus. I saw this patient in the office, with Dr Senear. We examined him carefully for lichen planus and finally came to the conclusion that he had lichen striatus.

DR LOUIE H WINER, Minneapolis This is the first case of lichen striatus I have seen with the exception of that in the case reported by Dr Senear and Dr Caro. I am pleased to see the histologic section, because what clinically resembled psoriasis or lichen planus turned out to be an entirely different picture.

DR M R CARO The clinical differentiation is rather difficult unless one has the history. The three diseases from which lichen striatus must be differentiated are nevus unius lateris, psoriasis and linear lichen planus. In the 10 cases which Dr Senear and I reported, the lesions disappeared without any treatment, local or systemic. The location of the eruption in all but 1 case was on the upper extremities. In the case of 1 woman it was on the neck. This is the first case we have encountered with the eruption on the lower extremities. This distribution is the exception to the rule that lichen striatus does not appear on the legs. Histologically all one finds is acanthosis, with slight intercellular edema. There are a few perivascular round-cells. The picture is much the same as is seen in chronic neurodermatitis. It is probably no more than a linear manifestation of neurodermatitis. There are many different theories to account for the localization in lichen striatus. There may be some congenital factor due to injury in the germ plasma. There is another theory that explains all cases of the disease on the basis of distribution of the nerves.

**A Case for Diagnosis (Staining of the Skin from Quinacrine Hydrochloride?)** Presented by DR J H MITCHELL

W H, a man aged 26, enlisted in the Army of the United States on March 3, 1941 and was sent to Panama. While there he took quinacrine, but he has taken quinacrine hydrochloride for the past two and one-half years. The past thirteen months were spent in the South Pacific. During his stay there lesions developed on the interdigital surfaces of the fingers and margins of the palms. These have not been pruritic, but they caused a feeling of stiffness. Some of the lesions occasionally became fissured. A few pustules appeared from time to time. The patient had not observed any similar lesions until he boarded the transport for home. Many of the men on board had similar lesions on the hands, and the impression seemed to be that the lesions on the hands were due to fungi. The treatment has been limited to potassium permanganate soaks.

There is a canary yellow tinge to the skin of the entire body, best seen in the bearded region and on the feet. There is also some staining of the nails.

On the interdigital surfaces of the thumbs and index fingers and to a lesser extent on the other interdigital surfaces are bluish red slightly hyperkeratotic nodules, split pea sized and smaller. There are two dime-sized, reddish brown, slightly keratotic lesions on the outer left ankle. The microscopic examinations did not show fungi. The histologic observations are consistent with the diagnosis of lichen planus hypertrophicus.

## DISCUSSION

LIEUT A R CUKERBAUM, U S N R, (by invitation) I have seen some of this discoloration of the skin due to quinacrine hydrochloride. I have never seen lichen planus. I think that the lesions are merely coincidental and are not part of the staining of the skin from quinacrine hydrochloride.

DR S J ZAKON Quinacrine hydrochloride is a synthetic product of the flavine group, as is acriflavine. It is sensitization to the sun that accounts for the discoloration.

DR L F WEBER The discoloration becomes generalized without exposure to the sun.

DR S J ZAKON In Europe the use of acriflavine caused a black discoloration of the skin. This could be a chemical phenomenon.

DR S ROTHMAN (by invitation) Two patients were presented at the February meeting who had been taking quinacrine hydrochloride, and both had lichen planus (ARCH DERMAT & SYPH 51 353 [May] 1945).

DR L F WEBER I should not accept quinacrine hydrochloride as being the cause of lichen-planus-like lesions, because in the 2 patients previously presented and whom I have seen in the clinic several times since the yellowish discoloration has disappeared.

DR M R CARO The 2 patients presented at the February meeting were husband and wife, who had taken quinine for malaria without any cutaneous symptoms. About a month before presentation they changed to quinacrine hydrochloride, and then lichen-planus-like lesions developed. The yellow discoloration has faded out, but the lichen-planus-like lesions are still present.

DR LOUIS A BRUNSTING, Rochester, Minn. My associates and I have used quinacrine hydrochloride extensively for the last few years in the treatment of malaria of the tertian type. In none of the patients has a yellow color developed, nor has there been a recurrence of the malaria.

DR J H MITCHELL There is an article in *The Journal of the American Medical Association* for Sept 23, 1943 (123 192) stating that in a large percentage of men taking quinacrine hydrochloride this color developed. The day that this man came in, I had a Major in the office who had also just returned from the Southwest Pacific. The photosensitizing effect of the sun is not borne out by the fact that this Major had the greatest amount of yellow color in the crotch. Both men had the characteristic coloring in the bearded region. There is no question that quinacrine hydrochloride causes yellow discoloration, because it has been observed in large numbers of persons. Dr Caro was kind enough to look at the slides in the case presented today, and he said that the changes were consistent with a diagnosis of lichen planus hypertrophicus.

DR M R CARO The changes present in the section are those ordinarily seen in lichen planus. The infiltrate is not as dense as in ordinary lichen planus, but

in the hypertrophic form this type of infiltration and edema is commonly seen.

**Pemphigus Vulgaris** Presented by DR DAVID V OMENS and (by invitation) DR HAROLD D OMENS and DR M OTSUKA

J H, an American engineer aged 60, presents an eruption of four weeks' duration, composed of bullae, varying in size from that of a pinhead to that of an egg or larger, some of which contain clear fluid while others have a lactescent content. The eruption started on the medial aspects of the extremities as a diffuse bullous eruption, which was thought to be a bullous type of multiform erythema. After a few days the eruption spread to the body, with systemic involvement except for the mucous membranes of the nose and mouth. There is no history of injury or of vaccination.

The examination of the blood showed a hemoglobin content of 67 per cent and 4,020,000 erythrocytes, the differential count was 52 per cent polymorphonuclear leukocytes, 21 per cent eosinophils, 20 per cent lymphocytes, 6 per cent monocytes and 1 per cent basophils.

**A Case for Diagnosis (Pemphigus, Dermatitis Herpetiformis?)** Presented by DR F E SENEAR and DR THEODORE CORNBLEET and (by invitation) DR H C ROLL

A man, aged 62, has had a bullous eruption for two months. The lesions start as central bullae, and there is peripheral progression. They heal and then recur. The bullae are hemorrhagic except for a few lesions on the chest and the right leg. There is no history of ingestion of drugs. The lesions itch severely. The cell count of the contents of the blister showed 16 per cent lymphocytes, 82 per cent neutrophils and 2 per cent eosinophils.

## DISCUSSION OF TWO PRECEDING CASES

DR C W LAYMON, Minneapolis These 2 cases bring up a question which has been under discussion for sixty years or more, whether dermatitis herpetiformis and pemphigus are the same disease or are different diseases. Before that time all diseases characterized by bullae were classified as pemphigus. About 1885 dermatitis herpetiformis was separated from pemphigus. It is surprising to note that there is no single absolute point in the differentiation. The itching, the presence or absence of the Nikolsky sign, the presence or absence of eosinophilia and the course of the disease are all points in the differentiation of the two diseases. I think that the first case presented is one of pemphigus vulgaris of severe type.

DR UDO J WILE, Ann Arbor, Mich. I have never seen new lesions occurring at the periphery of older recessive lesions in any case of dermatitis herpetiformis in which the possibility of pemphigus was suggested. That is something that is characteristic of pemphigus. I wonder if any one else has encountered that in pemphigus. The second patient had zoster-like bullae at the site of his previous hernia.

DR OTTO FOERSTER, Milwaukee I agree with Dr Wile. In Vienna pemphigus pruriginosus was the diagnosis for what the Americans call dermatitis herpetiformis.

DR H E MICHELSON, Minneapolis It is true, as Dr Laymon brought out, that one cannot make a differentiation by a single criterion. That is why so many theories have been presented in the hope that some one can make a complete differentiation.

DR FRANCIS W LYNCH, St Paul It is my impression that there is no difficulty in differentiation in younger persons. The difficulty is in patients of 60 and more, in whom the lesions are dense and the individual lesions are large enough to be those of pemphigus. While a therapeutic test is never a good diagnostic criterion, in a few patients whom I have seen of the older group there has been no response to the sulfonamide drugs, either sulfadiazine or sulfathiazole, while in the younger group the response is fairly constant.

DR DAVID V OMENS In the last month I have seen about 6 patients with pemphigus and in no two of them was the course of the disease the same. When I first saw this patient he presented a large dense bullous eruption on the inner aspect of the arms and around the neck. After a few days it involved the body. I immediately hospitalized him, and he has gone rapidly downhill. In another patient whom I treated for dermatitis herpetiformis for a few weeks a bullous eruption developed. I thought that it was pemphigus and gave him acetarsone, and he is doing well.

DR THEODORE CORNBLEET Eosinophils are produced by the presence of histamine in the blood, and certain cells are converted into the eosinophilic type. It is interesting that the first man had comparatively little itching, and yet 21 per cent of his leukocytes are eosinophils. In our patient there were only 2 per cent eosinophils in the bullous content, and he had severe itching. It is certainly true that all dermatologists have had the opportunity of seeing many patients with bullous eruptions presenting themselves as having erythema multiforme, dermatitis herpetiformis and pemphigus. Not knowing what to tell the patient or his family, the dermatologist would like to have some successful test produced which would tell him, if not the exact diagnosis, certainly the prognosis. Thus far, there is certainly nothing one can do about it.

### Rosacea and Rhinophyma (Nose and Ear Lobes)

Presented by DR F E SENEAR and (by invitation)

DR P K WEICHSELBAUM

This 43 year old bartender presented himself at the University of Illinois College of Medicine with rosacea and numerous papules and pustules, involving the entire face except the periorbital region. The skin of the nose is red and hypertrophied and presents numerous patulous follicles. The ear lobes are similarly involved and are convoluted to give the impression of more swelling than is actually present. The eruption began eight years ago on the cheeks and then involved the nose and the rest of the face. The patient has a papulopustular eruption on the sternal and interscapular regions. He also has stasis ulcers on the left external and internal malleoli.

The dermatitis on the face has improved considerably with the use of 40 per cent sulfur ointment.

#### DISCUSSION

DR THEODORE CORNBLEET I am of the opinion that this man has hypertrophy of the ear lobes. On palpating the ear lobes one finds that they are cupped and that the convex surface is really that of a sphere.

DR P K WEICHSELBAUM (by invitation) Dr Senear and I have never seen anything similar to this involvement of the lobe, so we thought that we would show it. I think the description Dr Cornbleet just gave is a good one.

### Pityriasis Rubra Pilaris (Vitamin A Deficiency)

Presented by DR OLIVER S ORMSBY

P S, a man aged 58, has had an eruption for four and one-half months. In the beginning the face and scalp were red and scaly but they have now cleared. The eruption is generalized and consists of keratotic papules and psoriasiform scaling patches. The keratotic spines on the abdomen protrude 2 mm above the cutaneous surface. The typical horny plugs are present on the dorsal surface of the fingers. There is a decided keratosis of the palms and soles. The skin of these areas is dull red and greatly thickened. The keratotic papules and follicular plugs are extensively present on the entire skin from the clavicles downward. There are no subjective symptoms.

#### DISCUSSION

DR LOUIS A BRUNSTING, Rochester, Minn. In this patient the disease is of short duration, if it continues longer, I believe that he will show the characteristic salmon discoloration of the face. It might be keratoderma climactericum of Haxthausen. While the disease is related to vitamin A deficiency, the answer does not lie entirely in that field, there are a number of things that enter into the picture. I believe that this man shows as well defined spinous lesions of a keratotic type as one will see. Some recent investigative work has emphasized the action of some other chemicals on vitamin A.

DR EDWARD A OLIVER It is interesting to see such a classic picture of pityriasis rubra pilaris. This man shows everything except the scaling eruption on the scalp and scaling on the face. I have had many cases which were discussed pro and con.

DR THEODORE CORNBLEET In line with what Dr Brunsting mentioned, I presented a classic case of pityriasis rubra pilaris in a little boy who had a deficiency of vitamin A. I tried alpha tocopherol in large doses, it helped some, but there was improvement only to a limited extent. Dr Ebert has also seen this patient, and I should like to ask him what other therapy has been used.

DR M H EBERT That patient was shown several months ago. Since the administration of alpha tocopherol he has had intramuscular injections of vitamin A. He has shown considerable improvement. The outlines of the old lesions are still visible, hence one can see exactly how much improvement has been made. He is certainly not cured but is improved.

DR DAVID V OMENS I saw 1 patient with pityriasis rubra pilaris who was treated with alpha tocopherol, with no beneficial results. In fact, in a period of three months not only did the child have a recurrence of the lesions, but they were much more severe. Since then he has been under treatment with Dr Finnerud and has had large doses of lard internally. The lesions cleared almost entirely in a short period. I wonder whether that form of treatment is not of some value in this type of case.

DR OLIVER S ORMSBY I presented the patient because the eruption was clinically classic but histologically not at all in line with ordinary pityriasis rubra pilaris. The patient is rather elderly to have this disease, which is usually seen in children or in women. The family history is not significant. I saw the patient yesterday for the first time, hence I shall have an opportunity to test the value of vitamin A for hyperkeratotic lesions.

DR M H EBERI This was an industrial case, and the question came up whether the disease was due to the occupation of the patient

**Dermatofibrosarcoma Protuberans with Dementia Paralytica Tabetic Type** Presented by DR EDWARD A OLIVER and (by invitation) DR SAMUEL M BLUEFARB

L J, a white man aged 40, first noticed the development of tumors on his back about twenty months ago. They grew fairly rapidly and attained their present size in a period of fourteen months. There has been no change in the size of the tumors in the past six months. The largest tumor is about the size of a fist, and it is solid, pedunculated and pale red. There are numerous satellite lesions ranging in size from that of a pea to that of a walnut. These tumors are not painful and cause discomfort only when pressure is applied. Bleeding occurs on the slightest trauma.

The patient is now being treated for dementia paralytica, tabetic type. He has previously had specific antisyphilitic therapy (total amount unknown), including nineteen injections of tryparsamide and sixty-six hours of malaria therapy.

The pupils are irregular and unequal and react sluggishly to light. The Romberg sign is present, and the patient is ataxic. The patellar and achilles reflexes are absent. The last spinal fluid examination showed a positive Kahn reaction, a colloidal gold curve of 432210000, a 1 plus reaction for albumin and 2 cells.

DISCUSSION

DR S W BECKER I thought that clinically this was a typical case as presented. However, some years ago Binkley wrote a paper on this subject (Binkley, G W ARCH DERMAT & SYPH 40 578-594 [Oct] 1939) and called attention to the fact that the lesions occurred in the nipple line. In this patient there are no lesions in that location. When I examined the sections they were typical of von Recklinghausen's neurofibromas and did not suggest dermatofibrosarcoma protuberans. The pathologists have called attention to the frequency of malignant degeneration in neurofibromas. I have never had occasion to see one. I wonder whether this could be of that type. Perhaps further biopsy studies would be enlightening.

DR M R CARO I had the same impression that clinically the case fitted in well with the diagnosis as presented but histologically it was one of neurofibromatosis.

DR EDWARD A OLIVER As I understand from reading the textbooks, there is no definite picture of dermatofibrosarcoma protuberans except that of fibrosarcoma. I read Binkley's paper and looked at his illustrations of the location of the lesions. It is true that in this patient the location is a little out of the ordinary, being in the midline of the back. In not all the cases of dermatofibrosarcoma that have been presented have the lesions been in the mammary line as Binkley pointed out. In a number of cases lesions have been seen in the upper part of the back as well as in the preclavicular area and in other regions not lined up with the mammary ridge. Dr Bluefarb and I were going to offer this as a case for diagnosis but then decided to present it under the diagnosis given.

**Cutaneous Neuroma** Presented by DR F E SEVEAK and DR M R CARO and (by invitation) DR C H STUBENRAUCH, JR

B V S, a Negro woman aged 46, noticed an infection near the left nipple in June 1943. It was incised

and drained of pus, and the wound healed rapidly. The patient remembers bruising the site in October 1943 after which it became painful and tender. The area has enlarged slightly, and the symptoms have persisted.

On the lower outer quadrant of the left breast near the nipple is an irregularly rounded dull reddish plaque about 2½ inches (6.3 cm) in diameter. The skin is smooth and unbroken, and it can be wrinkled slightly. The entire plaque is firm, and the induration extends deeply. There is slight tenderness on pressure.

The histologic examination of a specimen removed from the plaque showed that the epidermis and upper part of the corium were approximately normal. The deeper part of the corium was composed largely of many round and oval masses of concentric fibrous tissue. Staining by silver impregnation showed the core of these bundles to be formed by nerve fibers, while the Van Gieson stain showed the surrounding fibers to be composed of collagen, and the Weigert stain showed the absence of elastic fibers.

DISCUSSION

DR UDO J WILE, Ann Arbor, Mich. Probably some of you will recall that at the meeting of this Society at Ann Arbor I had the temerity to show a patient who had what appeared to be a simple keloid of the breast. No one had any idea at all from the clinical appearance that it was anything other than a keloid. She had so much pain of a distinctly neuritic character that I performed a biopsy and, to my great surprise, found that it was a cutaneous neuroma. From that time to this I never encountered another case. With a background now of 2 cases, perhaps this Society will uncover more.

DR M J REUTER, Milwaukee. I am not disputing the diagnosis but merely wish to point out that a lesion of the breast which appears to be inflammatory may be carcinoma. That was my first impression on seeing this lesion. It looks inflammatory, at least, there is local heat and redness. I believe that there are inflammatory-like changes in the breast which are due to carcinoma, and biopsy should be performed on any inflammatory lesion of the breast that does not heal in two weeks.

**Nevus Pigmentosus et Pilosus** Presented by DR L F WEBER and (by invitation) DR C H STUBENRAUCH JR

B P, aged 9 weeks, had a brownish pigmentation of the dorsum of the left hand at birth. The area of pigmentation has gradually extended to involve the fingers, wrist and palmar surface of the hand. No other congenital defects have been observed.

The skin of the dorsum of the left hand, the left wrist and most of the left palm is brownish black and sharply demarcated from the normal skin of the forearm. There is an excessive growth of moderately coarse hair in the involved area. Soft papillary excrescences are present, especially on the fingers and the back of the hand.

The patient is presented chiefly for suggestions as to therapy.

DISCUSSION

DR LOUIS A BRUNSTING, Rochester, Minn. It seems to me that the only thing to do is to wait until the child is older and then to consider excision and skin grafting.

DR DAVID V OMENS. Why wait until the child is older, the lesion will take in a larger cutaneous area.

DR FRANCIS W LYNCH, St Paul. There is little to be gained by operating on this child at the present

time There is a possibility that there are changes in the deeper structures, and there may be a lack of development that will be evident later

DR. L. F. WEBER My problem was to treat or not to treat and I debated the question pro and con It seemed to me that in performing a plastic operation one was apt to interfere with the movement of the fingers later I thought of using solid carbon dioxide One reason I am hesitating is that some deformity of the fingers may result later, which may be more objectionable than the nevus is at the present time

**A Case for Diagnosis (Melanoma?) Presented by DR. HERBERT RATTNER**

A physician, aged 35, presents sharply defined pigmented lesions on the lips, which have developed gradually They began on the left side five years ago and on the right side one year later They have not increased in size, and there are no subjective symptoms There is no history of injury or of ingestion of drugs

**DISCUSSION**

DR. S. W. BECKER I have seen a few of these lesions and have performed biopsy on a couple of them The microscopic section simply shows overactivity of normal pigment There is no increase in the number of melanoblasts These lesions started five years ago and have not grown for four years I simply call them lentigines I questioned the man carefully and learned that he sunburns easily There is no reason to do anything with the lesions, though they are superficial

DR. JOHN F. MADDEN, St. Paul The first question is whether this is melanoma or melanosis, the answer to which can be determined by biopsy After that, if it is decided that this is not a melanoma, the next problem is choice of therapy Regardless of what Dr. Becker says about the harmlessness of the lesions, they do annoy the persons who have them I have treated the few patients whom I have seen with solid carbon dioxide, and in some of them the lesions have disappeared completely In others a ring formed on the opposite side of the area on which the solid carbon dioxide was used The lesions will respond to other treatment besides solid carbon dioxide or cautery I had the unfortunate experience of having them extend beyond the wounds I have made

DR. HERBERT RATTNER Dr. Pusey used to freeze them off I have seen these lesions successfully removed by treatment with solid carbon dioxide

**NEW YORK DERMATOLOGICAL SOCIETY**

A. BLINSON CANNON, M.D., *President*

GEORGE C. ANDREWS, M.D., *Secretary*

*April 25, 1944*

**Tuberculosis Miliaris Disseminata Faciei Presented by DR. FRED WISE**

M. B., a man aged 42, was previously presented before the Manhattan Dermatologic Society on April 11, 1944 by Dr. Max Scheer for diagnosis and with a questioned diagnosis of dermatitis medicamentosa due to bromides The patient later denied that he had taken Bromoseltzer

Subsequent investigation showed that the sedimentation rate was 7 mm per hour An intradermal injection

of old tuberculin, in a concentration of 1 to 5,000, elicited a negative reaction A roentgenogram of the chest showed "thoracic asymmetry from marked rotary curvature of the dorsal portion of the spine and central tubercle scars of old puerile type"

A nodule removed from the face was diagnosed by Dr. Charles F. Sims as tuberculosis cutis In describing his observations, he said that the epidermis was somewhat flattened, with obliteration of some of the rete pegs A dilated follicle filled with a horny plug was noted In the middle and deep parts of the corium there was a diffuse cellular mass, composed of epithelioid wandering connective tissue and small round cells, with some plasma cells The epithelioid cells were arranged at many points in tubercle formation Numerous thin-walled dilated vessels filled with blood were seen dispersed throughout the cellular mass The larger vessels were dilated and their walls edematous Their intimal nuclei projected into the lumens of the



Distribution of lesions in a case of tuberculosis miliaris disseminata faciei

vessels Basophilic degeneration of the collagen in the upper part of the corium was noted

The patient is being treated with general ultraviolet irradiation of the body and with intravenous injections of 10 mg of gold sodium thiosulfate, the dose to be gradually increased

**DISCUSSION**

There was unanimous agreement with the diagnosis

**Keloid Following Herpes Zoster Presented by DR. EUGENE F. TRAUB**

E. G., a boy aged 5, had an eruption which was first noticed on or about Nov. 10, 1943, on the chin and left side of his face and which extended into the scalp It was diagnosed by his family physician as impetigo, and it consisted of rather deeply seated vesicles on an inflammatory base The patient was sick at the time, and during the course of the disease two lower teeth on the left side were lost, the mouth and tongue were



swollen and there was some eruption on the left buccal mucosa. The patient had a fever but experienced no pain. Rather, he had an itching sensation at the sites of the lesions. The disease ran its course in about four weeks, and as the lesion on the chin healed and the crust came off a thickened keloidal scar was noted at the site. This continued to grow until it reached its present size.

There is now on the chin a hard firm keloidal mass, measuring about  $1\frac{1}{2}$  inches (8.8 cm) in diameter. The scarred areas, anterior to the ear, have healed without keloid formation.

The patient has had no previous treatment except for one dose of roentgen rays administered to the chin the day before presentation. His case is presented as one of healed herpes zoster that had apparently involved the second and third divisions of the trigeminal nerve, followed by the unusual complication of the loss of several teeth and the formation of a keloid in a boy who at the time was not quite 5 years old.

#### DISCUSSION

DR PAUL E. BECHET. The keloid is unusually extensive for having developed over such a brief period. The two most important therapeutic approaches to consider are, first, to excise the lesion with the cutting current and follow this with a single massive dose of roentgen rays and, second, to use roentgen rays alone in moderate doses. It would be possible to obtain excellent results in this particular instance with doses of 751, unfiltered, at weekly intervals for seven to ten weeks.

DR ANTHONY C. CIPOLLARO. I have not been particularly impressed with the results obtained in treating keloids with roentgen rays. An excellent result can be obtained by a plastic operation. I believe that the operation would not involve too much risk or the sacrifice of too great an amount of tissue. I favor plastic operation for treating this lesion.

DR MAURICE J. COSTELLO. I wonder whether this result was influenced by medication, such as applications of solution of gentian violet medicinal, which have been known to cause ulceration and scarring. I suggest treatment with roentgen rays.

DR FRED WISE. I am strongly in favor of treatment with roentgen rays to the exclusion of other methods.

DR GEORGE C. ANDREWS. I agree with Dr. Wise. The keloid is of such short duration that I should not rush into any drastic treatment at this time. With conservative treatment I think that it will gradually disappear.

DR HOWARD FOX. As this lesion is comparatively recent, it should be radiosensitive. I strongly favor a trial with roentgen rays, and if such treatment is not successful one can always have a plastic operation performed later. There are other interesting features of this case. Herpes zoster in a child of 5 years is uncommon, especially when it involves both the second and third divisions of the fifth nerve. There is a history of rather severe constitutional symptoms, which favors the diagnosis of zoster as opposed to impetigo. It should be added that in children under 10 years zoster usually does not cause pain.

DR FRANK C. COMBES. I agree with those who think that roentgen ray therapy is indicated in this case.

DR R. H. RULISON. I agree that roentgen ray treatment is probably the treatment of choice. For the last two or three years I have been treating keloids with small doses, frequently over a period of several months, and I believe that the results have been satisfactory.

I think that a keloid as young as this should respond to roentgen therapy.

DR GEORGE M. LEWIS. I am not certain that I have followed all the points given in favor of herpes zoster to the exclusion of pyoderma of some type. The loosening of the teeth and the fact that keloids often follow pyoderma are in favor of the view that pyoderma preceded the formation of the keloid.

DR JOHN C. GRAHAM. I certainly should use roentgen rays and in comparatively minute doses. I feel certain that a good cosmetic effect will result.

DR EUGENE F. TRAUB. The patient and I are appreciative of the various suggestions that have been made for treatment. The factors that seemed to me to favor the diagnosis of herpes zoster are, first, that the eruption was entirely unilateral, involving the second and third divisions of the fifth nerve and, second, that it had consisted of about a half-dozen groups of lesions of various sizes, extending up the left side of the face well into the scalp, leaving scarring on the cheek anterior to the ear and the large keloid on the chin. There were no scars, nor was there loss of hair on the scalp. Another factor that would exclude a diagnosis of a pyogenic infection was the loss of two teeth, the swelling of the tongue and the fact that there was some eruption on the buccal mucosa. All these factors taken together should certainly exclude a diagnosis of an ordinary pyogenic infection, although of course it is possible that the reason for the development of the keloid from the lesion on the chin was because of the slow healing occasioned by some pyogenic infection. I have seen this patient only on one previous occasion and have given him one roentgen ray treatment. My experience has been somewhat similar to that of Dr. Cipollaro—that roentgen rays do not always leave the excellent cosmetic result one is led to expect. By that I mean that frequently keloids, especially one as hard as this and made up of as much scar tissue as this one appears to be, may require enough roentgen ray treatment to leave a certain amount of sequelae before the keloid has been entirely reduced. As this patient is a child, and hence should perhaps respond better than an adult, the lesion, which has been present for almost five months, can hardly be regarded as an early process, I believe. In my opinion an early keloid is one that is only a few weeks old and certainly not over one to two months old. This patient will be given a moderate amount of roentgen ray treatment, and if the lesion does not respond surgical intervention will be considered.

DR FRANK C. COMBES. I should like to ask a question. I have sometimes thought that I had better results with radium than with roentgen rays in these cases. Has that been any one else's experience?

DR EUGENE F. TRAUB. This was my thought also. If it is necessary to irradiate this lesion sufficiently in attempting to flatten it for sequelae of the roentgen therapy to remain, I believe that such could not be considered good therapy.

#### A Case for Diagnosis (Acrodermatitis Continua, Psoriasis?) Presented by DR GEORGE M. LEWIS

F. C., a man aged 58, was previously presented at the Manhattan Dermatologic Society on April 11, 1944.

#### DISCUSSION

DR GEORGE C. ANDREWS. I am in favor of the diagnosis of arthropathic type of psoriasis. The lesions on the scalp and the hands are typical.



DR FRID WISE I agree with the previous speaker I should not have been able to make this diagnosis if I had not observed similar cases before I have seen the arthropathic type of psoriasis with the same kind of deformities of the hands and feet as are seen here

DR MAURICE J COSTELLO The diagnosis of psoriasis arthropathica was suggested when this patient was previously presented, at the Manhattan Dermatologic Society I am now in favor of that diagnosis, especially since a lesion has developed on the patient's nose suggestive of psoriasis

DR EUGENE F TRAUB While a number of the lesions on this patient suggest the diagnosis of psoriasis, on the whole the lesions on the hands, especially about the finger nails, suggest a pyogenic process of some type Therefore, before a diagnosis of psoriasis can be accepted as final in this case one should certainly have some microscopic proof

DR JOHN C GRAHAM I believe that it is psoriasis

DR R H RULISON I think that it is psoriasis

DR FRANK C COMBES I am not sure just what this is The patients with arthropathic psoriasis whom I have seen have always been much sicker than this man is I have not seen a patient with such a disease walking around, apparently in good health The patch on the scalp, of course, looks much like psoriasis, and there is no doubt that the patient has an atrophic arthritis Whether they are both a part of the same process, I do not know

DR HOWARD FOX I agree with Dr Combes that patients with the disease known as psoriasis arthropathica are in poor physical condition I prefer to diagnose this disease as a combination of psoriasis with the atrophic form of arthritis (arthritis deformans)

DR GEORGE M LEWIS The history of injury prior to the onset of the disease and the sequence of the appearance of one lesion followed by that of others seems to be fairly typical of acrodermatitis rather than of psoriasis The psoriasis-like lesions on the scalp and nose certainly suggest that the lesions on the hand may also be psoriasis Atrophic arthritis accompanying psoriasis is often painless This man is trying to get compensation by claiming that he was injured when a splinter ran into his finger and that the disease now present is resultant He received roentgen ray treatments to the hands before consulting me

#### **Papulonecrotic Tuberculid Including Involvement of the Face, Chest and Back Presented by DR MAURICE J COSTELLO**

I saw J F, a girl aged 19, born in New York city of Spanish parentage, for the first time on March 25, 1944 She stated that she has had an eruption for the past two years Her parents are living and apparently are well One sister is dead, the living sister has had tuberculous lymphadenitis and scrofuloderma for years The patient had a roentgenogram of her lungs a year ago which did not show evidence of tuberculosis

The patient has a generalized symmetric nonpruritic eruption involving the extensor surfaces of the arms, hands, legs and feet It also involves the face (including the eyelids eyebrows and ears), the chest and the back The eruption on the extremities is typical and consists of matchhead-sized to dime-sized lesions in all stages of development, including small evolving papules and papulopustules necrotic lesions and cicatrices, with erythema and hyperpigmentation, some of which are punched out and pale

The eruption on the face, chest and back on casual observation looks like acne, but there are no comedos,

the skin is not oily and there are lesions on the eyelids and helices of the auricles The lesions are miniatures of the larger lesions on the extremities The scars are small and pitted There are no oral lesions, but there is a whitish scar on the soft palate near the anterior margin of the fauces A hazelnut-sized lymph node can be palpated in the right anterior cervical region, a month ago it was the size of a robin's egg

The Vollmer tuberculin patch tests on the inner aspects of both arms elicited positive reactions in the form of solid follicular papulovesicular lesions which persisted for one month An intradermal injection of 0.05 cc of tuberculin in a concentration of 1 to 5,000 elicited a 4 plus reaction The patient's temperature and her pulse and respiration rates were normal, and if it were not for severe fronto-occipital headaches she would enjoy excellent health She states that the eruption almost completely disappears in the summer

Biopsy of an entire evolving papule (3 by 3 mm) surmounted by a pinhead-sized pustule, which was taken from the inner aspect of the left leg, revealed these facts Throughout the middle and upper parts of the cutis the vessel walls were swollen, and there was a pronounced focal cellular reaction In one area there was a diffuse cellular infiltration beneath the epidermis The epidermis overlying this part was somewhat acanthotic, the granular layer was missing, and the surface was covered with a large crust The intima of the vessels was swollen, and in many areas in the vessel wall were necrotic and broken down The cellular infiltration was composed of small round cells, wandering connective tissue cells and many polymorphonuclear leukocytes This picture could be due to some systemic disease, and if necrosis of the entire area ensued, the diagnosis of papulonecrotic tuberculid would be appropriate

Treatment thus far has consisted of two roentgen ray treatments of 75 r each to the right side of the face and neck, the external aspect of the right elbow region and the lateral aspect of the right leg, ankle and foot One injection of 0.006 Gm of dichlorophenarsine hydrochloride (Winthrop) was given intravenously

#### **DISCUSSION**

DR HOWARD FOX The lesions on the elbows and legs are classic ones of papulonecrotic tuberculid If I had seen the facial lesions alone, I should not have thought of this disease

DR PAUL E BECHET In view of the objective symptoms, it would be impossible to disagree with the diagnosis, even the pitting on the face is characteristic However, there are a number of exceedingly small, pinhead-sized to pinpoint-sized lesions that suggest acne rather than papulonecrotic tuberculid The patient's skin is oily, and I believe that there is a mild acne on her face besides the papulonecrotic tuberculid

DR MAURICE J COSTELLO I believe that the lesions on the face, chest and back are the same as the other typical lesions on the extremities There are no comedos, there are lesions on the eyelids, and a number of lesions are present on the helices, which are uncommon locations for acne There is also the fact that the lesions on the face appeared at about the same time as the lesions on the extremities

#### **A Case for Diagnosis (Psoriasis of the Nails?)**

Presented by DR GEORGE M LEWIS

R B, a man aged 47, first noticed a small cutaneous lesion in July 1943 This initial lesion occurred on the side of the heel Several other scaly red areas appeared, after which a disease developed on the nails of the

great toes and later spread to the nails of all the toes and fingers. The cutaneous eruption responded to local treatment, but the disease of the nails has persisted. The latter is characterized by the change in the nail proximally with the growth outward, finally producing complete change in the nail. As this process is completed, the entire nail becomes ridged longitudinally and is porous and lusterless with a considerable loss of substance.

Examinations for fungi gave negative results.

#### DISCUSSION

DR HOWARD FOX. My father used to record cases like this as simply "nail disease." He did this after he had excluded paronychia, fungous or other infection, congenital malformations and dermatoses of the surrounding parts of the fingers. In his earlier days he did not have to speculate about endocrine substances and vitamins as possible causes of the eruption. One speculates on these subjects, though it does not help one's diagnostic ability to any appreciable extent.

#### A Case for Diagnosis (Angioma Serpiginosum?)

Presented by DR FRANK C COMBES

H W., a man aged 59, presents a vascular type of eruption, of four years' duration, symmetrically distributed on his arms, thighs and buttocks. Some of the lesions have partially faded. They are not elevated and are well defined with an irregular border suggesting geometric figures, typical of mycosis fungoides. Some lesions are spotted with varying degrees of erythema and areas of cyanosis. On closer inspection the patches, which approximate 20 to 30 cm in diameter, are studded with angiomatous puncta, occurring in groups extending peripherally, forming circular clear areas centrally. There is no purpura, the patches disappearing almost entirely on pressure. In some areas there is a fine, branny scale and a suggestion of atrophy. At no time have there been any subjective symptoms.

#### DISCUSSION

DR GEORGE C ANDREWS. I did not see any lesions of angioma serpiginosum. The lesions looked to me like eczematous lesions.

DR EUGENE F TRAUB. There are some peculiar features about several of the lesions in this patient. What appears to be a tiny deeply seated inflammatory pustule is surrounded by a zone of clear and apparently normal skin. This process occurs at three or four sites. The patient apparently feels that some of the lesions are pustular because he suggested that they might be secondary either to slight scratching or friction of clothing. I believe that this patient has some type of eczematization but certainly not angioma serpiginosum.

DR FRED WISE. I could not see anything that resembled the conditions in the cases of angioma serpiginosum which I have observed, of which there have been only 3 that were real outstanding instances of the disease. In this case the patient has no circles or rings or telangiectasia or shiny spots that resemble atrophic macules or scaling. I cannot offer any other diagnosis, however. It is possibly an eczema or a fungous eruption.

DR HOWARD FOX. I agree with Dr Wise that this eruption does not suggest a diagnosis of angioma serpiginosum, nor do I think that it is an eczematous eruption. It suggests the possibility of parapsoriasis in patches.

DR R H RULISON. The lesion did not conform to my impression of one of angioma serpiginosum. I have no diagnosis to offer.

DR FRANK C COMBES. I have encountered only 1 case of proved angioma serpiginosum. If this case is not one of that disease, I do not know what it is. There is no resemblance of the lesions to eczema, the lesions do not itch, and at no time has there been any vesiculation. In many places there are angiomatous puncta all over the lesions, which have spread slowly, leaving clear ringlike areas. During the last six months I have watched these lesions develop. There is no evidence of telangiectasia, the background being erythematous. It is my impression that occasionally this type of lesion may disappear spontaneously and that no therapy is of avail. This is contrary to Dr Wise's impression, who, incidentally, has written the best article on this disease that appears in English literature. I shall have a section of tissue removed for histologic study.

#### A Case for Diagnosis (Keratosi Bleunorrhagica?)

Presented by DR GEORGE C ANDREWS

H C., a man aged 39, complains of an illness dated from Dec 14, 1941, which started with nonspecific urethritis. Previously he had been treated for neuro-circulatory asthenia and for hydrops of the left knee joint.

On Jan 6, 1942, the sclera became injected, fever was present, there was difficulty in breathing through the nostrils, and a sore mouth, swollen gums and a sore tongue developed. He had arthritic pains in his left instep and twinges in both knees.

When examined, the conjunctivas were injected. The nasal mucous membrane was hyperemic. The mucous membrane of the mouth was also injected. The gums were swollen and dull red, and they looked as though they would bleed easily but did not. The tongue was heavily coated, with clean patches here and there. This coating finally desquamated, leaving a purplish glistening slightly edematous smooth surface. The tonsils had been removed. The peritonsillar nodes were slightly enlarged and tender. The lymph nodes of the groins were palpable, but there was no general lymphatic enlargement. The heart, lungs and blood pressure were normal. The abdomen was symmetric, and the liver and spleen were not enlarged. There was no local tenderness or muscular rigidity.

There was an erythematous patch about the size of a nickel around the meatus of the glans penis and another, the size of a dime, on the coronal surface. These patches were well defined and slightly scaling.

The deep reflexes were all normal. The left instep was splinted with adhesive tape and was slightly tender, and the base of the left great toe and both knees were slightly tender. Later, fluid appeared in the right knee, and the shoulders became really painful.

A few days later definitely palpable and well defined hemorrhagic nodules appeared on the bottom of the left great toe. Later the soles became studded with similar palpable hemorrhagic nodules, varying in size from that of the head of a white-headed pin to that of a small pea. Sulfathiazole was given for six days without benefit.

A centrifuged specimen of urine showed pus cells and large numbers of epithelial cells. The prostate was normal. In the glass test of the urine the content of the second glass was clear while that of the first glass included a few epithelial and pus cells, slightly more than normal. Smears and cultures were made and repeated three times. There were no gonococci in the smears, and all cultures of material from the urinary tract from both the bladder and the anterior urethra,

were negative for pathogens except for a growth of *Staphylococcus albus*

The Kahn reaction was negative on two occasions. Culture of the blood was negative. Smears and cultures of material from the mouth showed no Vincent organisms. The usual organisms, *Staphylococcus*, *Streptococcus* and *Pneumococcus*, were cultured from the mouth, but none predominated.

The rectal temperature was 101.8 F on admission to the hospital. Three days later it reached 103 F and five days later, 104 F. For four days it was just above 100 F and during the remainder of the patient's three weeks' stay in the hospital the temperature was between 99 and 100 F, except for the last seven days, when it was normal. The differential blood counts, even with the temperature normal for a week, continued to show a leukocytosis, and the last blood count, on Feb 2, 1942, showed 17,000 leukocytes, with 45 per cent myeloblasts and 19 per cent myelocytes.

A letter from Dr George Minot, who saw the patient in Boston, says in part "Mr C has presented a most interesting and unusual problem. It does not seem to us here that he has leukemia, as we have seen no myelocytes or grossly immature white cells in the blood. The blood has been examined on several occasions. The white cell count has been in the vicinity of 16,000. Although the differential count has naturally varied somewhat, it has always been essentially the same.

"It is of course very interesting that you observed some myelocytes, and I cannot help wondering if the appearance of myelocytes in the blood might have been the result in some way of the sulfonamide drug that he took. It would be unusual in a person with leukemia to have the leukemic blood vanish, and I feel that he must have had a leukemoid reaction. I am, indeed, at a loss to explain that picture.

"Dr Schwartz, one of our competent dermatologists, considered that the picture resembled blenorrhagic keratosis.

"Dr Richard Chute, one of our genitourinary surgeons, felt that the patient had probably not had gonorrhea, because the urethritis had occurred about twelve days after possible exposure. Dr Chute was able to obtain only a small amount of excretion on prostatic massage, and culture of this material yielded no organism that resembled gonococcus."

Seven weeks ago the patient had another attack, beginning again with urethral discharge, followed in three or four days by aphthous stomatitis and severe conjunctivitis. He then came to me. The pharynx and palate were diffusely hyperemic, and there were scattered aphthae. There was injection of the conjunctivas, most pronounced at the outer margins. There was an exfoliation of the skin of the soles, and the toe nails were thickened and uplifted from the nailbeds.

Both cultures of the urethral discharge showed *Staphylococcus albus* and a few diphtheroid bacilli. Urethral smears showed a moderate number of pus cells and a few gram-positive cocci. Broth cultures of material from the mouth demonstrated the presence of hemolytic *Staphylococcus aureus*. Examination of a hanging drop preparation was negative for *Trichomonas*. Scrapings from the soles and toe nails contained mycelium, and cultures showed the fungus to be *Trichophyton gypsum*.

Today the patient presents a subungual abscess of the left index finger and of the right great toe nail, but the conjunctivitis and pharyngitis are greatly improved. However, the urethritis and pustules and ulcers on the glans are present. The blood count on April 25, 1944, showed 99 per cent hemoglobin, 5,120,000 erythrocytes and 12,500 leukocytes, with a differential

count of 66 per cent polymorphonuclear leukocytes (61 per cent mature and 5 per cent immature), 29 per cent lymphocytes, 3 per cent eosinophils and 2 per cent monocytes. There were no basophils.

#### DISCUSSION

DR FRANK C COMBES. It is difficult to say what this is without considerable study. As Dr Andrews read the history, I thought of keratosis blenorrhagica, and the lesion on the glans penis has the waxy appearance of some of the lesions one sees in that disease. I am at a loss to say what the lesions of the mouth are. I have seen such lesions in the mouth of patients with this disease but never with the diffuse stomatitis that this man presents.

DR HOWARD FOX. I suggest that a culture for diphtheria organisms be made.

DR R H RULISON. This is a puzzling case. I think that perhaps Dr Fox's suggestion that the causative agent may be some diphtheroid bacillus with a predilection for the mucous membranes is a valuable one. My idea is that this patient has some double infection, a symbiosis of some kind, which accounts for the difficulty.

DR GEORGE M LEWIS. It looks to me like an infection, possibly cutaneous and oral diphtheria, and that would explain the clinical features.

DR G F MACHACEK. I still think that the patient is taking a drug, particularly in view of the stomatitis.

DR EUGENE F TRAUB. From the history of sudden onset and the peculiar lesions on the mucous membranes I thought of a drug eruption, but I do not believe that any drug could account for the lesions of the mucous membrane and the paronychia and the penile lesions. For this reason I think that some type of infection is the more likely explanation.

DR FRED WISE. I cannot offer a diagnosis, but I feel that the diagnosis rests with the bacteriologist.

DR GEORGE C ANDREWS. I shall make the cultures suggested. I made cultures of material from the lesions over a week ago and got no growth. I did not use Loeffler's medium, but I made them on dextrose broth and on Sabouraud's medium. I shall make special cultures on Loeffler's medium and on a special medium for the *Gonococcus*. The complement fixation test is so unreliable that it is now seldom used.

NOTE.—Shortly after the presentation of this case the article describing Behcet's syndrome appeared in *The Journal of the American Medical Association*. This case is now considered an instance of Behcet's syndrome.

#### American Leishmaniasis Presented by DR HOWARD FOX

V F W, aged 35, a federal purchasing agent, has spent the last two years in Brazil, much of the time in the Amazon valley. During the previous eight years he spent six months of each year in Brazil.

About a year ago he had a penile lesion in which spirochetes were found by Dr Mota, of Rio de Janeiro. He was then given a course of twenty-four intravenous injections of oxophenarsine hydrochloride and an equal number of intramuscular injections of a bismuth preparation. No serologic tests were made at that time.

An eruption appeared in January 1944 for the first time, and it consisted of lesions appearing one after another on different parts of his body. The first lesion appeared on the right ala nasi, followed by one on the right side of the neck and others on the extremities and back. They were bilateral and asymmetric. He now presents a total of eleven lesions, all of the same

type They are indolent button-like lesions, with central ulceration, covered by adherent brown crusts The borders are slightly elevated and reddish Many of them show a reddish areola  $\frac{1}{8}$  to  $\frac{1}{4}$  inch (0.3 to 0.6 cm) in width The eruption appeared while he was receiving antisyphilitic treatment

He was seen by Dr Joseph Earle Moore, who referred him on March 22, 1944 Biopsy performed by Dr Ketron was reported as showing a granuloma consistent with the histologic structure of syphilis On the basis of this report, that the eruption might be syphilis resistant to treatment with arsenic and bismuth, the patient was treated by Dr Moore, at Johns Hopkins Hospital, with penicillin Two million units was administered during a ten day period As the result of this treatment was a failure, the patient was referred for an opinion as to the possibility that his lesion was a tropical dermatosis

Microscopic examination of scrapings from an ulcer, stained by Wright's method, failed to show leishmanias

Treatment with antimony and potassium tartrate was advised He received his first injection today

Examinations made at Johns Hopkins Hospital showed that the urine was normal and the blood count included 5,000 leukocytes, with a differential ratio of 56 per cent neutrophils, 40 per cent lymphocytes and 4 per cent eosinophils Results of complement fixation and flocculation tests for syphilis were positive

NOTE—When the patient was last seen, the lesions were healing rapidly

#### DISCUSSION

DR FRED WISE I should not have thought of the diagnosis of syphilis as the lesions appeared today They resemble the biskra button lesions I have seen in Colombia

DR MAURICE J COSTELLO This case is similar to the one that Dr Fox presented seven years ago before this Society (ARCH DERMAT & SYPH 37 888 [May] 1938) That patient had more numerous lesions with involvement of the mucous membrane of the mouth and destructive scarring of the nose The eruption gradually disappeared after he had received injections of antimony and potassium tartrate

#### Psoriasis, Pseudopelade (Lichen Spinulosus), and/or Alopecia Areata Presented by Dr G F Machacek

J L, a woman aged 38, is presented from the Vanderbilt Clinic She has had psoriasis for eight years and alopecia for two years The patient sought treatment on Feb 9, 1944, at which time a large oval area of alopecia, about 3 cm in diameter, was noted in the occipital region Other scattered areas of alopecia were present Some were covered by psoriatic lesions, and others were free The large area over the occiput now appears to be somewhat atrophic It is from this area that a specimen for biopsy was taken The left elbow shows an oval plaque, also about 3 cm in diameter, which was covered by silvery scales of a psoriasiform nature The initial diagnosis was psoriasis and alopecia areata

At this time there is a psoriatic lesion of the left elbow, which no longer shows the same degree of desquamation as on admission There are numerous areas of alopecia, varying considerably in size The large occipital area shows some degree of atrophy Residual evidences of psoriasiform lesions are noted Some of the areas of alopecia are completely free from evidence of inflammatory change One area discloses follicular keratinization

The serum cholesterol level was 296 mg per hundred cubic centimeters The cephalin flocculation test showed no floccules The basal metabolic rate was —9 per cent The Wassermann reaction was negative Biopsy revealed keratinization of dilated follicular funnels, with atrophy of the epithelial lining and perifollicular lymphocytic infiltration—lichen spinulosus

Treatment consisted of application of crude coal tar, compound ointment of sulfur N F to the areas of alopecia and exposure to ultraviolet rays She received 4 to 6 Lexo wafers (each wafer containing 3 Gm of soybean lecithin, 1,000 U S P units of vitamin A, 100 U S P units of vitamin D, 165 U S P units of thiamine and 81 mg of phosphorus) daily

#### DISCUSSION

DR FRANK C COMBES I agree with the diagnosis

DR MAURICE J COSTELLO I wonder if Dr Machacek thought of the diagnosis of lichen planopilaris, because the type of baldness this patient presents is also associated with erythema, scaling and follicular keratoses

DR G F MACHACEK I think that it might be considered to be the same picture as lichen planopilaris

#### Papular Sarcoid of the Face Presented by DR FRED WISE

M C, a woman aged 47, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 11, 1944, presenting lesions of six months' duration She stated that she had never had any serious illnesses and that she has been in good health except for "high blood pressure" She gives no history of tuberculosis She has four children, who are "healthy" The lesions are painless

A few papules appeared on the right side of the face six months ago Three months later the other lesions developed None has undergone regression Scattered over the face, more pronounced in the central portion and on the left cheek, are discrete matchhead to pea sized yellowish nodules, totaling about twenty-four They are easily compressible with a diascopic glass, leaving distinct yellow spots

The routine laboratory tests revealed no abnormalities except a slight eosinophilia

A nodule was removed and examined by Dr Charles F Sims He interpreted it as sarcoid In the description of his observations, Dr Sims said that the epidermis was somewhat thinned, with obliteration of the rete pegs and corresponding papillary bodies In the upper part of the corium was a well defined cellular mass, consisting for the most part of epithelioid cells surrounded by a very sparse small round cell infiltration No central necrosis was visible The vessels of the upper part of the corium were dilated and surrounded in part with a mild cellular infiltrate, composed of small round and plasma cells Basophilic degeneration of the wall of the upper part of the corium was noted While these observations are consistent with a diagnosis of tuberculosis miliaris disseminata faciei, the absence of necrosis and the sparse inflammatory masses surrounding the tubercles favor the diagnosis of sarcoid

#### DISCUSSION

The members agreed unanimously with the diagnosis

#### Lupus Pernio (Besnier) Presented by DR JOHN C GRAHAM

M K, a woman aged 36, from Brooklyn Hospital dispensary, has had what she calls chilblains for many years Two years ago she first noticed tenderness of her right little finger Her symptoms are always worse in the winter and improved during the summer,

but they never disappear. She complains of a burning sensation and soreness.

Examination shows a fusiform swelling of the right little finger, with purplish discoloration and a slight ulceration at the tip. She says that she has lost the nail several times.

On the arms, legs, cheeks and ears the patient presents purplish areas, only a few of which are slightly indurated. The purplish macules vary in size up to that of a finger nail. On diascopic pressure occasional brown nodules are demonstrable. Also, two weeks ago the patient had a hemorrhage from the lungs and spit up two mouthfuls of bright red blood. She has a cough and she says that she catches cold easily. However, she is gaining weight. Roentgenograms of the chest have not as yet been made, but an examination by the medical department disclosed no definite physical signs in the lungs. The patient also has a group of flat warts on the back of the right hand.

#### DISCUSSION

DR FRANK C COMBES. With the exception of the solid, almost gangrenous area on the little finger, the whole eruption looks like erythema pernio and erythrocyanosis crurum.

DR PAUL E BECHET. The patient presents a clinical picture which I have not infrequently observed at various dermatologic clinics, and in the cases observed the picture was similar in every instance, namely, the presence of soft infiltrated violaceous to dusky reddish brown variously sized lesions, mostly on the extremities. There is no pain on pressure, and the infiltration is soft, and the lesions do not break down as in erythema induratum. They occur anteriorly as well as posteriorly, and while the dark color is accentuated by cold, the lesions appear as frequently in warmer weather. The persons in whom they occur are almost invariably young women with colorless faces and lackadaisical mien. From the clinical appearance and course of this eruption I believe that it is not related to erythema pernio, nor is its clinical picture and course that of tuberculosis cutis. I usually regard this type of manifestation as being tuberculoid in character and possibly as being related to the tuberculids, despite the fact that involution leaves some slight scarring (but not varioliform, as in papulonecrotic tuberculid).

DR EUGENE F TRAUB. This patient appears to have tuberculosis, but I believe that the eruption on the lower extremities, if not also the one on the little finger, is largely based on some type of vascular disease. Therefore, I suggest that she be studied in a clinic devoted to vascular diseases rather than that we debate the dermatologic name to be appended to her condition.

DR FRED WISE. I have the same impression as Dr Bechet, that this woman has a form of tuberculosis of the skin, whether one can find the bacilli or not. Whether it is a lupus pernio or what Dr Machacek called "Hutchinson's chilblain lupus," I am not able to say. I think that she should be treated on the basis of a tuberculous infection.

#### A Case for Diagnosis (Urticaria Pigmentosa [Acquired Type]?) Presented by DR GEORGE M LEWIS

G V, a woman aged 54, is presented from the New York Hospital. She has had an eruption on her body for the past ten years. At times it becomes lighter. There are no subjective symptoms.

On examination the rash is erythematous and purpuric reticulated diffusely over the trunk and ex-

trimities. Whealing can be established in both normal and affected skin.

The Wassermann reaction was negative. The urine was normal. The platelet count was 190,000, and the erythrocyte, leukocyte and differential counts were within normal range. The bleeding time was one minute two seconds. The report of a biopsy, performed at another hospital, has not yet been obtained.

#### DISCUSSION

DR HOWARD FOX. I think that this is a classic eruption of urticaria pigmentosa of the adult type. The lesions are red and small and are all of the same size. The associated dermatographia does not militate against the diagnosis.

DR FRED WISE. I agree with what Dr Fox said. It is a typical urticaria pigmentosa. If I were asked to make a differential diagnosis before a group of students between that and any other disease, I should be hard pressed to think of any other diagnosis worth discussing.

DR GEORGE M LEWIS. The case is unusual because (1) the patient shows dermatographia, which I do not think is typical of urticaria pigmentosa, (2) not all the lesions are discrete and (3) there are purpuric areas in retiform configuration. I believe that the presence of dermatographia may be used as a differential point between urticaria with pigmentation and urticaria pigmentosa.

#### Erythema Presented by DR FRED WISE

S W, a woman aged 34, was presented before this Society on March 28, 1944 (ARCH DERMAT & SYPH 53 124 [Aug] 1945).

The case turned out to be an instance of a true vasculitis with definite inflammatory changes in the blood vessels, with telangiectasia, but I have not yet come to any conclusion about what the diagnosis is. It is not just a functional change in the skin.

#### A Case for Diagnosis (Angioma?) Presented by DR FRED WISE

A F, a boy aged 10 years, was presented before this Society on March 28, 1944 (ARCH DERMAT & SYPH 53 127 [Aug] 1945).

The entire lesion was excised and was interpreted by Dr Charles F Sims as "angioma which may fit in with hemangiopericytoma (Stout)." In describing his observations he said that the epidermis revealed no noteworthy changes. In the upper and middle parts of the corium were numerous dilated irregular blood vessels lined with a thin endothelial lining. Surrounding these vessels was a variable mantle of cells, which in most instances appeared to be spindle shaped. Mitoses were not visible. Some of the vessels contained serum and red blood cells. No free hemorrhage into the surrounding collagenous framework was seen.

The specimen was sent to Dr Stout, who has previously reported cases like this. His diagnosis was hemangiopericytoma.

#### Lupus Erythematosus of Occupational Origin Presented by DR R H RULISON

S P, a man aged 59, was presented before this Society on Feb 29, 1944 (ARCH DERMAT & SYPH 51 292 [April] 1945).

The patient is improving with a fair amount of speed under treatment with injections of a gold salt, which tends to confirm the diagnosis of lupus erythematosus.

# NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

DAVID BLOOM, M.D., *Chairman*

GEORGE M. LEWIS, M.D., *Secretary*

May 2, 1944

## A Case for Diagnosis (Infectious Granuloma [Tuberculous, Syphilitic?]) Presented by Dr F. P. LOWENFISH

A de B., a man aged 45, is presented from City Hospital with a lesion on the left zygoma which has been present for thirteen months. Thirteen months ago the patient noted a swelling over the left zygoma and consulted a dentist, who extracted a wisdom tooth. While he was under the care of this dentist, several pieces of bone were also removed from this region. Since then the swelling and a draining sinus have persisted. About three months ago a nontender, noninflamed swelling appeared on the back. This was aspirated and 30 cc of purulent material removed, which was found by smear and culture to be sterile.

In 1917 the patient had a penile sore and was treated for several months in Cairo, Egypt, for syphilis. In June 1943, he was again treated for syphilis and received eight injections of arsphenamine, twelve of silver arsphenamine, twenty-four of a bismuth preparation and fifteen of mercuric succinimide. From February to April 1944, he received fourteen injections of mercuric succinimide and ten of oxophenaisine hydrochloride (mapharsen).

Smears and cultures were negative for actinomycetes. Biopsy by Dr. Machacek was reported as showing infectious granuloma of unknown cause.

Röntgenologic examination revealed (1) a destructive lesion of the left zygoma, (2) filling of a fistulous tract extending up to the destructive lesion of the zygomatic process (visualized by injection of iodized poppyseed oil) and (3) advanced hematogenous type of bilateral pulmonary infiltration.

### DISCUSSION

DR OSCAR L. LEVIN: The lesion over the left zygoma is simply the opening of a sinus leading down to the bone. It is not characteristic of a specific disease. It is a result of chronic inflammation and probably due to infection of the bone. On the back there is an area of serpiginous, irregularly grouped lesions suggestive of a healed syphilitic eruption. I see no evidence of tuberculosis.

DR GEORGE M. LEWIS: I think that actinomycosis still has to be considered in this case, despite the negative results of smear and culture. There is no positive evidence of any other disease. The granulomatous appearance and discharging sinuses are typical of actinomycosis.

## Generalized Progressive Scleroderma with Nodules Presented by Dr ABRAHAM WALZER

D. W., a white woman aged 46, born in Greece, first presented herself at the dermatologic clinic of the Beth Moses Hospital in February 1944, for a rash on the upper part of the trunk and a "stiffness" of the fingers and the face.

The patient has had asthma for about twenty-three years and hoarseness for many years. Ten years ago she was operated on for an ectopic pregnancy. From

Jan 8 to 28, 1944, she was in the Beth Moses Hospital for hematemesis. While there, frequent blood counts, determinations of blood chemistry and examinations of urine showed no abnormalities. The Wassermann reaction of the blood was negative. The stools showed no evidence of blood. Roentgen examination of the chest and stomach revealed nothing abnormal, and she was discharged with the cause of the hematemesis undetermined.

The rigidity of the fingers, the inability to open the mouth and the formation of the cutaneous lesions began at about the same time four years ago. The skin on the face is hard and cannot be picked up easily. The face is expressionless, and motion of the mouth is limited. The fingers move with some difficulty and are partly fixed in a semiflexed position. The skin over them is thin and tight and seems to be bound down to the underlying structures (sclerodactylia).

The cutaneous lesions appeared first on the right side of the neck and have been extending ever since. They are now present on the neck, chest, back, breasts, shoulders and arms and scattered here and there in other locations. They are nodular and vary in size from that of a pea to that of a dime. Some are round, others are oval or elongated. The skin over them varies in color from that of normal skin to red or dark brown. The nodules are numerous and close together, producing skin that is tight and bound down to the underlying structures.

Histologic studies of one of the nodular lesions showed no changes in the epidermis. In the papillary layer and in the corium there was a fairly pronounced fibrosis. The connective tissue bundles ran parallel to the skin. The vessels were congested and showed a mild perivascular infiltration of lymphocytes and polymorphonuclear leukocytes. The sebaceous glands, coil glands and hair follicles were not affected.

### DISCUSSION

DR FRED WISE: I am unable to suggest a more acceptable or plausible diagnosis than that offered by Dr. Walzer. There is no question that the patient has a hidebound condition of the skin on the fingers, but the lesions on the body are not those that one can accept as a form of scleroderma. They appear to be solid fibromas.

DR OSCAR L. LEVIN: This is the most interesting case shown this evening. The patient presented various lesions. I was interested in the hoarseness, and I think that she probably has lesions of the larynx. She shows diffuse pigmentation, hardening and inelasticity of the skin as observed in scleroderma. The nodules are larger than those of lichen nitidus. There are tender papules, especially on the back of the hand, that are of the size of a pinhead to that of a lentil, slightly elevated and of a grayish white tint. To me they suggest the lesions of calcinosis cutis. The whole clinical picture is that of a pluriglandular disturbance with various changes in the skin. I think that further studies of the endocrine system and of the calcium metabolism should be made, particularly because of the occasional presence of calcium deposits in scleroderma. I believe the nodules are calcium deposits in the skin.

DR ABRAHAM WALZER: The question of nodules occurring in association with scleroderma is extremely rare. The surface is usually smooth, but in morphea, as Dr. Wise suggested, raised lesions due to hypertrophy of connective tissue will occasionally be found. In diffuse scleroderma, however, nodules do not usually occur. In 1937 a report of a case resembling this one was published (Butler, J., and Layman, C. W.). Nodular



Diffuse Scleroderma, *ARCH DERMAT & SYPH* 35:919 [May] 1937) Their patient was a man about 70 years old who for about six months had had lesions consisting of multiple split pea-sized nodules on the forearms, neck and chest. The fingers were tight, so that he could not grasp objects, and the skin over the entire body became stiffer than normal. The histologic study showed increase in the blood vessels with sclerosis of the larger ones. There were pronounced fibrosis and sclerosis. These changes were not specific for scleroderma, but the authors could visualize the case as an instance of an early stage of that disease. They reviewed all cases reported in the literature from 1906, and were able to find only about 8. Of these, Lipshutz' case of sclerodactylia with nodules and Bruhn's case of scleroderma in bands with nodules were the most typical.

In the case presented tonight, definite sclerodactylia is present with nodules on the upper part of the trunk and on the extremities. The histologic picture of the nodules is not that of typical scleroderma but rather of a sclerosis. I thought the best title for this case would be scleroderma with nodules, leaving the origin of the latter still open. My idea, however, is that it belongs in this group of rare cases of nodular scleroderma and that these nodules are in all probability a variation of scleroderma. The suggestion that the lesions result from injections for asthma can be disregarded when one considers the number of the nodules and the fact that the patient had only a few injections.

#### Localized Myxedema Presented by DR OSCAR L. LEVIN and DR JESSE A. TOLMACH

S. C., a man aged 26, is presented from Beth Israel Hospital with an eruption of the legs which has been present for about nine months. He was treated at another hospital in September 1941 for hyperthyroidism with exophthalmos. At that time he had a diffuse soft, cystic bilateral swelling of the lower part of the neck anteriorly. The basal metabolic rates then were plus 29 and plus 21 per cent. An electrocardiogram on Sept 8, 1941 revealed left axis deviation. A subtotal thyroidectomy was performed on Sept 25, 1941. He was discharged from that hospital on October 12, in good condition, with the final diagnosis of exophthalmic goiter.

On the anterior surfaces of the lower ends of both legs there are now seen large, elevated plaques with a yellowish red tint. The surfaces are uneven and made up of pea-sized to walnut-sized nodular masses. The masses are tense and suggest edema, but there is no pitting on pressure. The follicular orifices in the patches are dilated. There are a few discrete papular strands on the middle third of the right leg above the large plaque. There is pronounced exophthalmos. The patient perspires freely but not as much as prior to his operation.

Laboratory examinations gave the following results. The urine was normal. A determination of the blood chemistry showed a cholesterol content of 179 mg per hundred cubic centimeters and a calcium level of 8.8 mg. The basal metabolic rate was — 30 per cent.

Biopsy showed the epidermis to be somewhat thin but otherwise normal, with a normal amount of pigment. The skin appendages were obviously atrophic. The opening of one hair follicle was wide and filled with keratinic masses. The fibers of the cutis were

show metachromasia. The corpus papillare and a narrow adjoining zone appeared normal in structure. They were also different from the remainder of the cutis in their staining reaction. They stained almost homogeneously with the Van Gieson stain, stained only faintly pink with mucicarmine, showed no metachromasia with polychrome methylene blue and stained pale pinkish with thionine. The histologic diagnosis was mucinous changes in the cutis.

#### DISCUSSION

DR FRED WISE. It is a typical case and corresponds to the cases described by O'Leary, of the Mayo Clinic. The interesting feature in this case is that the disease is probably due to hypothyroidism, if one accepts the statement that most of the thyroid has been removed surgically and that the lesions appeared afterward. The question of therapy is interesting.

DR E. WILLIAM ABRAMOWITZ. There are several interesting features in the development of localized myxedema in connection with hyperthyroidism. In the majority of cases the disease develops postoperatively. No one knows the cause of the development of these lesions in typical toxic diffuse goiter. I do not think the parathyroids should be blamed, because histologically the cutaneous lesions are due to a deposit of a mucinous substance. As a rule they are not associated with a generalized myxedema. The basal metabolic rate in these patients will vary, in most instances it is +30 or 40 per cent or more, only occasionally is it minus. Some patients have been operated on for hyperthyroidism, and it has not successfully reduced these lesions, which seem to be so resistant to all forms of treatment. The strong point against the influence of the parathyroid glands is the fact that there are patients with such lesions who have not been operated on and who have had no injury to these glands. I had occasion to see a patient with severe hyperthyroidism at Gouverneur Hospital who had not been operated on at all. The lesions looked like erythema nodosum. That patient was operated on later and died in a thyroid crisis.

DR JESSE A. TOLMACH. Localized myxedema may be seen both in hyperthyroidism and in hypothyroidism. As in this case, it sometimes occurs in cases of hyperthyroidism following thyroidectomy. This is the second case I have observed in which this has occurred. Reports in the literature in regard to therapy for the pretibial type of circumscribed myxedema are most discouraging. In answer to Dr Wise, treatment with thyroid should be employed very cautiously. In this case we tried small doses of thyroxin and the patient lost 10 pounds (4.5 Kg) in one week. There was no effect on the lesions, and this treatment had to be stopped.

DR OSCAR L. LEVIN. The patient shows symptoms of hyperthyroidism, which is a part of the general pluriglandular disorder as well as the dysfunction of exophthalmic goiter. The thyroid and other endocrine glands as well as the vegetative nervous system are affected. A patient may show evidence of hypothyroidism or hyperthyroidism during the course of the disease, and symptoms of both conditions may coexist. In this patient with exophthalmic goiter and evidence of hyperthyroidism there are also lesions of hypothyroidism, such as circumscribed myxedema of both legs.



active to produce secretions that played a part in the production of the symptoms of toxic diffuse goiter. Is it not possible that after the thyroidectomy these cells became hyperactive in a compensatory manner and subsequently caused symptoms of hyperthyroidism? Finally, as a result of overactivity these cells may have suffered from exhaustion and degenerated to develop ultimately into circumscribed myxedematous nodules and plaques.

#### Recurrent Syphilis, Macular Atrophy Secondary to Syphilis Presented by DR J LOWRY MILLER

J L, a 22 year old Puerto Rican man, is presented from the City Hospital, to which he was admitted complaining of a penile sore of three weeks' duration. He stated that he had a penile chancre which on dark field examination in 1936 was positive for spirochetes. Accompanying the chancre was a secondary rash which healed, leaving scars. He was admitted to a hospital and remained there for four months, during which time he had about sixteen injections in his arm and sixteen in his hip. Since discharge he has attended a syphilis clinic at irregular intervals, receiving an occasional injection into the arm and hip. The Wassermann reaction of the blood was said to be negative six months ago.

Examination shows a wide, firm, raised, indurated area around the corona, with two shallow ulcers in the centers. The left testicle is soft. Scattered over the trunk in a symmetric arrangement are many pea-sized whitish, atrophic areas.

Dark field examination of material from the penile ulcer revealed *Treponema pallidum*. The Wassermann reaction of the blood was 4 plus with cholesterol antigen and 4 plus with alcohol antigen. Frei and Ducrey tests elicited negative reactions.

Treatment has consisted of daily injections of ophthalmic hydrochloride, for a total of 108 Gm to date.

#### DISCUSSION

DR LOUIS CHARGIN. I do not think that there is any question about the macular atrophy, and with the history there is no doubt that the patient has syphilis.

#### Pyoderma, Perifolliculitis Capitis Abscedens et Suffodiens, Folliculitis of the Extremities Presented by DR GERALD F MACHACEK

A S, a Negro man aged 41, is presented from City Hospital, with lesions of the head, forearms, thighs, legs, buttocks and pubis of eighteen months' duration.

This is the patient's second admission to City Hospital, where he was first seen in 1933 after the development of a rash of the body which resulted in sycosis of the face, folliculitis of the scrotum and pubis and suppurative axillary adenitis. After incision and drainage, excision, skin grafting and roentgen ray therapy, he was finally discharged in 1935 with scars of the face, neck and axillas.

About eighteen months ago the patient applied a hair straightener (Conkolin), and a pustule of the left occipital region developed. Suppurative lesions spread over the scalp, resulting in scarred, bald, raised, boggy areas, many of which contained numerous orifices exuding pus. A generalized suppurative follicular eruption is seen on the hairy parts of the upper and lower extremities, the pubic region and the buttocks.

On the patient's first admission the Wassermann reaction of the blood was positive, and it is still slightly positive. Bacteriologic examination disclosed and still discloses *Staphylococcus albus* and diphtheroid bacilli from scattered lesions of various parts of the body.

Treatment has consisted of surgical incision and drainage, sulfathiazole locally and by mouth and wet dressings.

#### DISCUSSION

DR FRED WISE. I think that attention should be called to the fact that this is an extremely rare disease and that this case is a true example of perifolliculitis capitis abscedens et suffodiens. Many cases presented with such a diagnosis are simply instances of ordinary folliculitis. Roentgen ray therapy produces a temporary alleviation of symptoms, whereas for ordinary folliculitis roentgen irradiation is not frequently required, since good results may be obtained with topical applications.

DR PAUL GROSS. This is an important case, showing the combination of what is called perifolliculitis abscedens et suffodiens, with lesions in the groin as seen in chronic pyoderma and considered by Melenev to be due to microaerophilic streptococci, and folliculitis of the legs. It supports the infectious cause of this much discussed dermatologic condition. I think that penicillin should be used in this case.

#### Von Recklinghausen's Disease in Identical Twins Presented by DR ABRAHAM WALZER

R S and J S, identical twin boys aged 6 years first presented themselves at the dermatologic clinic of the Brooklyn Jewish Hospital about two months ago for a rash that has been present since birth. There are two older children who are perfectly well. There is no one else in the family with similar lesions.

The cutaneous lesions of the children consist of tumors of the skin and pigmentation in J S and pigmentation only in R S. The tumors are of various sizes, shapes and consistency. Some project above the surface of the skin while others can only be felt. They vary in size from that of a pea to that of a hazelnut or larger. Most of them are covered with normal skin, while others are covered with skin that is slightly blue. Most of the tumors are hard, but some are soft.

The pigmentation consists of large, pale brown patches of various sizes and shapes and smaller dark spots, scattered over the trunk and extremities. A few hairy nevi, together with some vascular nevi, are also present.

There is no evidence of any involvement of internal organs. Physically and mentally, both children are apparently normal.

#### DISCUSSION

DR DAVID BLOOM. Dr Walzer is to be congratulated for presenting identical twins with von Recklinghausen's disease, for, as far as I know, no cases of its occurrence in twins have ever been reported in the literature. Collection and study of the cases of identical and of nonidentical twins with this disease may contribute considerable knowledge, and dermatologists should watch for such instances and report them or present them at society meetings. It is of interest that while both of the boys presented tonight show cafe-au-lait spots, only one of them shows tumors along the forearms and wrists. The parents deny having any cutaneous lesions, although thorough examination may reveal lesions which are overlooked by the layman. Assuming that the parents are not affected, these twins present the first generation in which the disease is manifested, for it is transmitted by the mode of simple dominance.

DR ABRAHAM WALZER. I could not find any reports of cases of von Recklinghausen's disease in twins. The mother says the nodules in the one boy have been

developing for the last year or so. In the beginning he had only the pigmenttd spots. I examined the parents and the other children and found nothing suggestive of the disease. There was no family history of any type of inherited cutaneous disease.

**Lichen Planopilaris, Lichen Planus et Acuminatus Atrophicans (Feldman) and Lichen Spinulosus and Folliculitis Decalvans (Little)** Presented by DR LEO SPIEGEL

S J, a schoolboy aged 15, born in the United States, was first seen at the Lenox Hill Hospital dispensary on March 21, 1944, with an eruption of about six months' duration involving the scalp, trunk and extremities.

On the scalp there are numerous patches of alopecia, mostly on the vertex and back of the scalp, giving a moth-eaten appearance. There is one large patch of alopecia, 8 cm in diameter, over the left parietal region. Itching has been slight, the chief complaint being the loss of hair.

Scattered over the scalp, neck, shoulders, arms, trunk, buttocks and extremities are slightly pinkish patches of various sizes and configurations, all patches are studded with acuminate keratotic papules, many of which show central plugs and are pierced by lanugo hairs. The hairy regions of the forearms show dime-sized areas of alopecia similar to the lesions on the scalp. The lesions on the trunk and buttocks are palm sized and larger, with small areas of normal intervening skin. All lesions are slightly raised and pinkish, and they give a nutmeg-like feel on palpation. The pubes and axillae are normal, as is the oral mucous membrane. No pustules have been observed at any time. The lesions on the scalp do not suggest atrophy.

Laboratory examination, including the Wassermann and Kline flocculation tests, gave negative results.

Biopsy showed a large, dilated follicle filled with a horny plug. In the lower portion about the follicle there was a moderate small round cell infiltration. There was some edema of the lower border of the wall of the follicle. The rest of the epidermis was somewhat acanthotic but otherwise showed no important change.

#### DISCUSSION

DR FRED WISE: This is a beautiful example of a disease, but it is not planopilaris. There is no evidence at all of lichen planus. If the patient had lichen planus in the mouth or lichen planus on the glans penis or had given a history of having had lichen planus, then the name "lichen planopilaris" would be justified. He has lichen spinulosus and keratosis pilaris of the glabrous skin, with an occasional lesion on the scalp. He now presents lichen spinulosus and lichen pilaris with an accompanying similar lesion of the scalp causing alopecia. It is a long title, but the term "planopilaris" is misleading in this instance.

DR PAUL GROSS: I was as hesitant as Dr Wise to accept Graham Little's view that all cases of lichen planopilaris represent a peculiar form of lichen planus, but a case which I observed several years ago taught me different. It was the case of a woman who was first seen with a mild eruption of typical lichen planus which responded to roentgen therapy. A few months later she returned to the clinic with patches of alopecia on the scalp and an extensive eruption of lichen spinulosus on the body lacking any clinical earmarks of lichen planus. Biopsy of a lesion of lichen spinulosus showed changes typical of lichen planus. I recall the case of another patient who was presented at a dermatologic meeting. This patient also had a widespread

eruption of lichen spinulosus, but on close examination small papules of lichen planus were recognizable surrounding some of the follicular spines. In my office I have treated a patient who in the course of a typical eruption of lichen planus acquired considerable lichen spinulosus in some areas but never showed any alopecia on the scalp. I do not deny that lichen spinulosus may develop under other circumstances, but I am certain that the syndrome present in this patient is lichen planus. It may require several biopsies to prove this diagnosis.

DR FRANK VERO: This case is extremely interesting. I failed to see lesions of lichen planus, but after long observation they may be seen. You may recall a patient that I presented here last year (ARCH DERMAT & SYPH 48:699 [Dec] 1943) showing all the symptoms of lichen spinulosus and lichen planus on the buccal mucosa and on the penis. I feel that in this patient lichen planus will ultimately develop.

DR E WILLIAM ABRAMOWITZ: This patient had gone to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital and also visited my office before seeing Dr Spiegel. It is difficult to make any positive statements about lichen planus because the cause still remains unknown and because of the vagaries of the so-called common type of lichen planus. Several years ago I presented 2 patients with lichen pilaris of the body and folliculitis decalvans of the scalp. In 1 of these patients lichen papules could be seen in a few places. The other showed none after long observation, but, instead, numerous pustules resembling some form of pyoderma developed on the scalp. The histologic picture in both cases was reported as lichen pilaris. I thought I made out some lichen planus papules on the penis in Dr Spiegel's patient. He seems to have improved with large doses of vitamin A. I agree with the diagnosis as presented.

DR OSCAR L LEVIN: The question is, has the patient lichen planus or lichen spinulosus? Lichen planus should be easily diagnosed by biopsy. I agree with Dr Wise that the patient shows generalized lichen spinulosus. As to therapy, lichen spinulosus is improved by the administration of vitamin A, and I have obtained the best results with large doses. I rarely use less than 150,000 U S P units daily for hyperkeratotic follicular conditions, and in this case I should give 300,000 units daily. I see no evidence of lichen planus.

DR LEO SPIEGEL: This patient's lesions are all of one kind, they begin as patches studded with acuminate follicles, pierced by hairs, and as the process advances the hair falls out. There are no subjective complaints, the patient's only complaint being the loss of hair. I believe this case belongs under the classification of lichen planopilaris as described by Sachs and De Oreo (Lichen Planopilaris, ARCH DERMAT & SYPH 45:1081 [June] 1942). There have been in all about 27 cases reported in the American literature, and some cases have been reported as instances of the disease even though the patients have not shown lesions of lichen planus. I thought I saw one papule suggestive of lichen planus on the penis. The patient has improved considerably, roentgen therapy has been given to the right arm. These areas show greater improvement than do other parts of the body.

**A Case for Diagnosis (Parapsoriasis, Secondary Syphilis?)** Presented by DR J LOWRY MILLER

G J, a woman aged 32, is presented from City Hospital, with a generalized eruption which has been

present for a year. One year ago an itching dermatitis developed in both cubital fossas which in the course of one month spread to involve the entire body except the face, palms and soles. The patient states that the rash varies in intensity from time to time but has never disappeared entirely. She says that she has taken no medicine by mouth.

The Wassermann reaction of the blood was 4 plus with both antigens on April 11, 1944, and the patient was admitted to City Hospital on April 19.

Examination shows a generalized, pea-sized to dime-sized, macular eruption. Slight scaling is present on many of the lesions. The larger lesions show some tendency to be arranged in the lines of cleavage. Vaginal examination shows nothing abnormal except a discharge. There are no lesions on the mucous membranes of the mouth. Results of serologic tests for syphilis were as follows:

|                          |         |          |          |
|--------------------------|---------|----------|----------|
| Wassermann (blood)       | 4/11/44 | 4/19/44  | 4/24/44  |
| Alcohol antigen          | 4 plus  | Negative | 1 plus   |
| Cholesterol antigen      | 4 plus  | 2 plus   | 3 plus   |
| Rabin precipitation test |         | Negative | Negative |

All dark field examinations failed to reveal *Treponema pallidum*.

Biopsy showed small nests of lymphoid cells in the upper part of the corium, with rare polymorphonuclear leukocytes and a few fibroblasts. The epithelium and vessels were normal. Nothing was seen suggestive of secondary syphilis.

#### DISCUSSION

DR LOUIS CHARGIN. I certainly do not think that the patient has syphilis. All the signs speak in favor of parapsoriasis.

### MANHATTAN DERMATOLOGIC SOCIETY

ANTHONY C. CIPOLLARO, M.D., *President*

WILBERT SACHS, M.D., *Secretary*

May 9, 1944

#### Nevus Pigmentosus et Pilosus Presented by DR MAURICE J. COSTELLO

M. T., a girl aged 16 months, has had a pear-shaped pigmented hairy nevus on the anterior surface of the right cheek since birth. She is presented for suggestions as to therapy.

#### DISCUSSION

DR FRED WISE. I suggest treatment with solid carbon dioxide.

DR E. WILLIAM ABRAVOWITZ. I treated 1 patient with electrodesiccation, with an unsatisfactory result. Carbon dioxide had been used before, and a keloid developed. I suggest, because of the presence of numerous hairs, excision of the lesion and replacement with a skin graft.

DR HERMAN SHARLIT. I recall that about ten years ago Dr. Ben Newman treated a nevus with solid carbon dioxide and metastatic melanocarcinoma developed.

DR HOWARD FOX. The case mentioned by Dr. Sharlit, which was presented before this Society by Dr. Costello, is the only one in which I have ever seen a malignant tumor develop after the use of solid carbon dioxide. I think that almost any treatment is safe for a hairy and pigmented nevus, and I agree with Dr. Wise that solid carbon dioxide gives the best results.

DR WILBERT SACHS. I believe that a nevocarcinoma cannot develop from any but a junction type of nevus.

DR FRED WISE. I have been successful in treating lesions of this type with solid carbon dioxide, and I have never seen any ill effects from it. I shave the hair first and then apply the solid carbon dioxide.

DR GEORGE M. LEWIS. I believe that treatment should be with solid carbon dioxide. An attempt should be made to treat the entire lesion at one time, so that even if the lesion is not blanched out entirely the result will be even. I have used the same technic as for removal of a keloid, making a tracing around the lesion on some transparent material, this outline is traced on a big piece of solid carbon dioxide, which is then shaped so that an exact replica of the lesion can be applied. I should not fear the development of malignancy either spontaneously or as the result of treatment.

DR DAVID BROOM. In the case mentioned by Dr. Sharlit, the plaque on the side of the nose of that young girl contained very short downy hairs, while in this case the hair in the nevus is long and fairly thick.

DR MAURICE J. COSTELLO. I presented the case referred to before this Society on Dec. 12, 1939, accompanying the presentation with a photograph (ARCH. DERMAT. & SYPH. 42:162 [July] 1940). The patient had a lesion similar to this except that throughout the lesion there were pinhead-sized areas of hyperpigmentation, darker than the background. It was covered with long lanugo hairs. It was treated by refrigeration with solid carbon dioxide and electrodesiccation, with an excellent cosmetic result. Six months later, coal black spots of hyperpigmentation could be seen in the center of the lesion. One of these, which gradually grew to the size of a pea, was examined microscopically and proved to be a melanocarcinoma. It was treated with radium by the late Dr. William Cameron, and the case was presented again, about four years ago. The patient is still alive and well, showing no evidence of spread of the disease. With regard to the case under discussion, I should be in favor of removal of the lesion by refrigeration with solid carbon dioxide if the lanugo hairs would also be destroyed by this method. Otherwise, I think that plastic surgery should be the method of choice.

#### Lymphoblastoma of the Scrotum Presented by DR MAX SCHELER

I. M., a married man aged 58, who was born in Russia, was first seen by me on April 28, 1944, complaining of a lesion on the scrotum, which had appeared eleven weeks previously. It began as a small nodule and has been steadily increasing in size. There are no subjective symptoms. The patient suffers from chronic pulmonary tuberculosis.

On the anterior surface of the scrotum is a firm infiltrated lesion, 3 by 4 inches (7.6 by 10.2 cm.), with a sharp border. The surface is redder than the rest of the scrotum.

The blood count was normal. The Wassermann reaction of the blood one month ago was negative.

A biopsy specimen, examined by Dr. Sims, was reported to be lymphoblastoma, either pseudoleukemia or lymphosarcoma.

#### DISCUSSION

DR WILBERT SACHS. I saw the section, and on hasty examination I am inclined to favor a diagnosis of lymphosarcoma rather than leukemia. If the lesion were the latter one would expect the vessels to be patent, while in this section they are closed.

DR HERMAN SHARLIT. I think that the lesion consists of a highly cellular infiltration which roentgen rays should eliminate.

**Nevus Comedonicus** Presented by DR E WILLIAM ABRAWOWITZ

A C, a woman aged 34, presents on the left side of the face a half-dollar-sized plaque, containing pinhead-sized to pinpoint-sized and lentil-sized deep pits, some of which contain comedos. The plaque has been present as long as the patient can remember.

DISCUSSION

DR DAVID BLOOM In most of the cases presented in the literature the lesions are not round, as in this case, but linear.

**A Case for Diagnosis (Dermatomyositis, Psychoneurosis, Dermatitis Medicamentosa [Pentobarbital Sodium], Cutis Marmorata?)** Presented by DR. GEORGE M LEWIS

M K, a medical secretary aged 34, is presented from the New York Hospital. She had poliomyelitis at the age of 4 and has had several corrective operations on the legs and arms. For the past three years she has had headache, backache, pain in the abdomen, pain in the bladder, painful and swollen elbows, epistaxis, low grade fever, sore throat, palpitations, dyspnea, extreme fatigue, burning tongue, night sweats, dizziness, nausea and vomiting, with frequent remissions and recurrences. There is a long family history of neurotic tendencies. She has recently had two attacks of an erythematous (edematous discrete symmetric rash, affecting the face, ears and extremities. The last attack began shortly after she had taken a capsule containing pentobarbital sodium.

The urine was normal. The white blood cell count varied on repeated examinations between 3,700 and 6,800. The Wassermann reaction of the blood was negative, and the blood sugar level was 86 mg per hundred cubic centimeters. Other routine tests revealed no abnormalities.

DISCUSSION

DR MAURICE J COSTELLO I believe that this patient has dermatomyositis with lupus-erythematosus-like lesions of the skin. She presents what to my mind is an important symptom—pain in the muscles of the calf when standing without shoes. It is almost impossible for patients suffering with dermatomyositis to walk in that manner. I think that the eruption is part of the dermatomyositis. Cases have been reported in which dermatomyositis has been accompanied with lupus-erythematosus-like lesions of the skin.

DR GIRSCH D ASTRACHAN I had occasion to observe a man of about 45 with recurrent attacks of erythematous lesions on his lower extremities and crooked patches on the glans penis. A blood count revealed a leukopenia (the white blood cells numbered 3,600). This improved after the administration of 3 drops daily of yellow bone marrow concentrate, and the eruption did not recur.

DR E WILLIAM ABRAWOWITZ I do not believe that this patient has any evidence of dermatomyositis now. The present eruption could be attributed to the administration of a barbiturate. That would be easy to prove by stopping the use of the drug and then giving her test doses of this and possibly other drugs that she may have taken.

DR JACK WOLF The extent and the nature of the eruption appear to favor the diagnosis of a drug eruption. This patient would be likely to take various drugs. The pains in the muscles of the calf may not be of any particular significance since the existing deformity would account for them.

DR GEORGE C ANDREWS One other test might be performed in this case. Patients with dermatomyositis if given a meat-free diet and then a certain amount of creatinine by mouth will excrete more than they are given. The test might be worth trying in this case.

DR ANTHONY C CIPOLLARO My impression is that this patient has lupus erythematosus of the acute disseminated type.

DR HOWARD FOX The patient has pain in a leg deformed by poliomyelitis. I should like to know whether the skin all over the body can be roughly handled without pain if the eruption is dermatomyositis.

DR WILBERT SACHS I understand that biopsy of the muscle showed no evidence of dermatomyositis.

DR GEORGE M LEWIS It is possible that the biopsy specimen was taken from the wrong muscle. I do not believe that dermatomyositis always shows generalized muscular involvement. Tenderness of the muscles seems to be variable. It may be constant in one patient and entirely absent in another. This patient has at various times had sensitive muscles, and, as Dr Costello remarked, the muscles of the calf are tender to touch now. I am gratified that no one thought the patient psychoneurotic. She willingly tells all about herself, saying that members of her family are neurotic and that she has more or less neurotic tendencies herself. I believe that she has a serious disease, though I am not entirely certain what it is. Some lesions appear to be typical lupus erythematosus. There were two acute episodes recently, which I am inclined to think were drug eruptions.

**Pyoderma Faciale Following Dermatitis Venenata** Presented by DR MAURICE J COSTELLO

M H, a woman aged 36, states that she applied to a skin-peeling and shelling institute for a skin peel on Oct 4, 1943. She was told by the proprietor that her scalp needed treatment and that she had acne. The proprietor advised several months' treatment before she was ready for the skin peel. The first treatment at the institute was given on Oct 20, 1943 and the last on March 10, 1944. She received three ultraviolet ray and two medicated mask treatments weekly. Some time during February a small red swelling appeared on the right side of the face below the lower lip. One of the operators in the salon squeezed a pimple, which caused the patient considerable pain. Some sort of medicine was applied. During the next few days new pustules formed, and the eruption began to spread on the right cheek. Within a few days it spread across the chin to the left cheek, and the patient was referred by the institute to a physician for treatment. He took material for a culture, opened many of the pustules and advised her to use solution of aluminum acetate. He prescribed a pill to be taken after meals. He also prescribed an antiseptic solution known as S T 37. His diagnosis was furunculosis. On April 6, 1944, there was intense inflammatory edema of the face, including the eyes, the cheeks, the neck and the upper half of the chest.

I saw the patient for the first time, on April 6, 1944, at which time she showed a severe eruption involving the cheeks, chin, neck, upper part of the chest and back. The eruption on the face consisted of numerous large painful cystic closely aggregated and coalescing papulopustules, with a superimposed dermatitis venenata, probably due to the application of hexylresorcinol (1:1000). Since that time treatment has consisted of hospitalization for controlled sulfathiazole therapy, and wet compresses of solution of boric acid,

lead-free solution of aluminum acetate and 3 per cent ammoniated mercury ointment were applied. The patient has greatly improved within the month.

While in the hospital, the patient had a hemoglobin content of 65 per cent, a red blood cell count of 3,800,000 and a white blood cell count of 12,600. Bacteriologic examination of the lesions on the face showed *Staphylococcus aureus* from one of the lesions and a long-chained *Streptococcus* from another.

**Purpura Annularis Telangiectodes (Majocchi's Disease?) Treated Successfully with Gold Sodium Thiosulfate** Presented by DR MAURICE J COSTELLO

C. C., a woman clerk aged 27, was presented for me by Dr Howard Fox before the New York Dermatological Society on Jan 26, 1937, as "A Case for Diagnosis (Majocchi's Disease?)" (*ARCH DERMAT & SYPH* 36 889 [Dec] 1937). She has suffered continuously from an eruption for the past thirteen years. The eruption is situated mainly on the lower parts of the legs, on the ankles and, to a lesser extent, on the thighs and the left forearm. The eruption is roughly symmetric and consists of areas of fine telangiectases from the size of a dime to that of a nickel. Pinhead-sized pecthiae are present at the periphery of these areas. The older lesions exhibit an atrophic, slightly depressed center, from the size of a millet seed to that of a pea. Surrounding this are numerous closely aggregated pinpoint-sized dots, which are brownish and which do not disappear on pressure. She has several spider nevi on her face.

The patient has had scarlet fever, pneumonia and rubeola. Her mother died of cancer. Her father is living and suffers from paralysis agitans. She has four sisters and two brothers, who are living and well. One sister had pulmonary tuberculosis but is now apparently cured.

Since her previous presentation the patient has visited several of the large dermatologic clinics in New York city. A diagnosis of Majocchi's disease is said to have been made by biopsy at one of them. She has had many forms of therapy since 1937, including local, systemic, climatic and physical. The application of fractional doses of low voltage roentgen rays offered no relief. Within the past four months the patient has received fifteen intravenous injections of 50 mg doses of gold sodium thiosulfate. For the first time in twelve years her legs are free of active lesions.

#### DISCUSSION

DR HOWARD FOX: I think that the question mark after the diagnosis should be removed. Majocchi's disease (purpura annularis telangiectodes) is rare, but it seems to me that this woman presents all the features indicated by the name of the disease. She has purpura, an annular eruption and telangiectases, and the eruption is on the legs, where Majocchi's disease usually occurs.

DR HERMAN SHARIT: To me it looks like superficial tuberculid.

DR FRED WISE: I think that the lesions are those of Majocchi's disease. One seldom encounters cases in which the lesions are as typical as those originally described by Majocchi, but I do not see how one can make any other diagnosis in this case. Even without the histologic description, the whole picture conforms to that of Majocchi's disease, and I think that it should be accepted as such.

DR WILBERT SACHS: The pathologic picture of Majocchi's disease is characteristic. When one finds

the characteristic features, I believe that there can be no question of the diagnosis. If this was diagnosed definitely as a case of Majocchi's disease with all microscopic features, I feel that that diagnosis will have to be accepted.

DR DAVID BLOOM: Has any study been made of the constituents of the blood or the state of the capillaries?

DR FRED WISE: In cases reported to date, there have been no notable changes in the metabolism or the blood picture.

DR MAURICE J COSTELLO: Results of all laboratory tests have been essentially normal in this case. I have the idea that the toxic agent in this case is probably from some tuberculous focus. I base that opinion on many factors, including the patient's response to gold sodium thiosulfate and the fact that several members of her family have pulmonary tuberculosis. I had to discontinue the use of gold sodium thiosulfate because of the development of stomatitis and an eruption, the first from gold that I have seen in private practice. I began treatment with 10 mg and increased the dose to 50 mg.

**Sarcoid, Late Secondary Syphilis** Presented by DR GERSH D ASTRACHAN

L. C., a man aged 37, born in Puerto Rico, was previously presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, on Nov 3, 1943.



Fig 1—Sarcoid of the penis

The patient was admitted to the Metropolitan Hospital, Welfare Island, on July 30, 1943, with an eruption on the face, upper and lower extremities, neck and penis of two or three weeks' duration. At the Metropolitan Hospital, the serologic tests were made nine times. The Wassermann reaction of the blood was negative on all occasions except one, on Oct 7, 1943, when it was 2 plus. The Kahn reaction, negative at the first two examinations, fluctuated thereafter from 1 plus to 3 plus. A serologic test performed at the

dispensary, on April 28, 1944, showed the Wassermann reaction to be plus-minus and the Kahn reaction to be 1 plus

Antisymphilitic therapy was instituted, but the patient could not tolerate dichlorophenarsine hydrochloride. He has received to date four injections of dichlorophenarsine hydrochloride and thirty of a bismuth preparation. The eruption showed a slight improvement on the legs and penis but became more pronounced on the neck, lips and chin.

A nasal smear examined on Nov 2, 1943, was negative for lepra bacilli. Reaction to tuberculin in a dilution of 1 to 10,000 was negative, on November 21.

Roentgenograms of the chest, wrists and ankles showed no evidence of abnormality.

Histologic examination of tissue taken from the right arm and the back of the neck showed both tissues to be histologically identical, consisting of portions of the skin in which the subcutis was filled with circumscribed foci of epithelioid cells. A few of these tubercle-like structures contained central zones of caseation necrosis and multinucleated giant cells of Langhan's type. The diagnosis of tuberculid of the skin (Boeck's sarcoid) was reported by Dr Jacob Taub who performed the biopsy.

The same slides were also examined by Dr Wilbert Sachs who found throughout the entire cutis numerous

of pigment in the basal cell margin. The diagnosis was late secondary syphilis.

#### DISCUSSION

DR HOWARD FOX I think that syphilis can be ruled out and that this is undoubtedly a case of hematogenous tuberculous infection that is seen at times in the Negro race. The case strongly suggests the one reported by Drs Bloom and Mendelsohn, in which there were lichen-planus-like lesions and other lesions which resembled keloids. Many of the lesions on the penis in this case certainly look like lichen planus, although the distribution of the eruption on the face is not like that disease. I think that there is no doubt that this is tuberculosis of the sarcoid type.

DR FRED WISE The diagnosis of sarcoid should be accepted on histologic evidence. Lichenoid sarcoid consists of papular lesions, not annular or discoid, it is a rare form of sarcoid which has not been exactly defined in the literature.

DR WILBERT SACHS The pathologic picture is definitely that of a sarcoid reaction. As to the question of lichenoid sarcoid, that is a clinical term.

DR DAVID BLOOM Dr Mendelsohn and I reported 2 cases, 1 of which is a replica of the case presented tonight. I believe that we have proved that these eruptions, seen almost without exception in Negroes, may be



Fig 2—Sarcoid of the arm and forearm

collections of epithelioid and giant cells (tubercles). In the center of many of these tubercles was necrosis. The walls of the vessels were thickened, and the intima was swollen. There was a sparse small round cell infiltration about the vessels. The overlying epidermis showed no important change. Within or about each tubercle was a small blood vessel. Against the diagnosis of syphilis was the lack of collarlets of plasma cells. Against the diagnosis of Boeck's sarcoid was the necrosis of the tubercles, the numerous giant cells and the changes in the blood vessels. Dr Sachs's diagnosis was late secondary syphilid or possibly a disseminated Boeck's sarcoid.

Histologic examination of a lesion from the penis (examined by Dr Andrew Saccone and Dr Wilbert Sachs) showed throughout the cutis small focal collections of epithelioid cells with some giant cells. There was a moderate cellular infiltration composed chiefly of small round cells with an occasional plasma cell. The blood vessels were somewhat dilated, the walls thickened and the intima swollen. There were blood vessels to be seen within or about the collections of epithelioid cells. The overlying epithelium showed no important change. There was a considerable amount

considered as a benign type of disseminated cutaneous tuberculosis. The fact that many of them develop during antisymphilitic treatment may possibly be due to the provocation of the tuberculous eruption by arsenicals.

DR MAURICE J COSTELLO I am impressed by the fact that in most cases of this type the eruption has been precipitated by antisymphilitic treatment. I should also like to ask Dr Astrachan what the tuberculin reaction is. Antisymphilitic treatment has been known to cause an exacerbation of pulmonary tuberculosis.

DR E WILLIAM ABRAMOWITZ If the patient has been treated with arsenicals, it might account for the lichen-planus-like lesions in the mouth.

DR GIRSCH D ASTRACHAN When I presented this case at the New York Academy of Medicine I considered three possibilities: late secondary syphilis, sarcoid and lichen planus. The last can be ruled out as a result of the histologic examination. Tonight I feel that one is dealing with a case of sarcoid. Whether or not the patient also has lesions of late secondary syphilis is difficult to say. There is no doubt, however, that he has a concomitant syphilitic infection. He has a persistently positive Kahn reaction. The last blood



tests, made a week ago, disclosed a 1 plus Kahn reaction and a doubtful Wassermann reaction. I believe that the lesions did not occur as a result of injections of arsenicals, because most of these lesions were present before the arsenicals were administered.

**Multiple Leiomyoma** Presented by DR ISADORE ROSEN

P. P., a man aged 52, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 26, 1944, with an eruption on the trunk of eleven years' duration.

On the back of the trunk at the level of the lower portion of the scapulas, there is a symmetric eruption of numerous reddish, oval and elliptic, pea-sized, fairly firm tumors, protruding above the level of the skin. They are arranged in the lines of cleavage. They are tender to pressure but in varying degree. On the lower lumbar and gluteal regions there are similar, but smaller, tumors, many of them skin colored, covered with wrinkled skin and not tender.

The laboratory examination confirmed the clinical observations.

DISCUSSION

DR FRID WISE: The lesions clinically resemble leiomyoma, but there is a slight deviation from those in the cases of it which I have observed. Some of this patient's nodules are more like fibromas—firm to the touch and not painful. I wonder whether there is a possibility of a mixture of fibroma with leiomyoma.

DR WILBERT SACHS: In studying the slide I found that the lesion has smooth muscle fibers, and I was not sure whether it was leiomyoma or neuroma. Certainly there is a neuroma present, and there may be a leiomyoma associated with it. In this section there are nerve fibers, hence it is not a pure leiomyoma. I believe that this lesion is more like a neuroma than a leiomyoma.

DR DAVID BLOOM: Because of the difference in tenderness in the lesions on the upper and lower parts of the back, biopsies of both kinds of lesions were requested. Has Dr Sachs seen any difference in the pathologic structure of these two tumors?

DR HOWARD FOX: I think that the lesions on the dorsal region are clinically typical of leiomyoma.

**A Case for Diagnosis (Pemphigus?)** Presented by DR FRID WISE

L. B., an American-born gentile 69 years old, referred by Dr Charles Kemm Good, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on May 9, 1944 presenting generalized bullous lesions of seven weeks' duration. He gave no history of previous eruptions. He has constantly been in good health. A prostatectomy was performed five years ago. His weight has been constant for the past five years. There are no subjective symptoms except some itching of the blisters after they burst.

A bulla first appeared in the front of the neck. Several bullae appeared a few days later on other parts of the neck, forehead, scalp, trunk and extremities, in the order named.

On the face, scalp, trunk and extremities, but mostly on the back, are discrete bullae, varying from the size of a match head to that of a cherry. Most of them are ruptured. They are tense and contain clear fluid, the walls are not firm but break easily on slight pressure. They all seem to arise from normal skin. There are no lesions in the mouth. The Nikolsky sign is absent.

The routine laboratory tests revealed no abnormalities except 8 per cent polymorphonuclear eosinophils and a vitamin C concentration in the blood plasma of 0.1 mg per hundred cubic centimeters (normal 0.7 to 1.4 mg).

A histologic study was interpreted by Dr Charles F. Sims as "a subepidermic bulla which may be consistent with pemphigus." His description follows: "In the center of the section is a large subepidermic bulla. The roof of the bulla is formed by the epidermis, which has become thinned with obliteration of the rete pegs. The floor is formed by the papillary bodies. Within the cavity one may note some fibrin and some scattered cellular infiltration composed of small round cells, wandering connective tissue cells, eosinophils, large lymphocytes and some polymorphonuclear neutrophils. The vessels of the upper part of the corium are moderately dilated. There is a diffuse and a perivascular cellular infiltration composed of cells similar to those described."



## Book Reviews

**Medical Uses of Soap A Symposium** By G Thomas Halberstadt, B S, Ch E, and others Edited by Morris Fishbein, M D Fabricoid Price, \$3 Pp 182, with 41 illustrations Philadelphia J B Lippincott Company, 1945

This book is a collection of sketchy discourses on the various detergents used to cleanse the skin, with particular emphasis being given to soap. The title, therefore, is somewhat misleading, not only in this respect but also with regard to the medical uses of soap, as no mention is made of its use in the preparation of pills, plasters and liniments, as an emulsifying agent or as an antidote for poison. The final chapter contains some data regarding its application other than as a detergent and keratolytic, but this section consists of but six pages of brief paragraphs culled from the literature of the last twenty years.

The subjects discussed are well chosen. The introductory chapter is devoted to a discussion of the various technologic aspects of soap, including its physico-chemical properties and those of soapless detergents. The author's description of the manufacture of the various types of soap, including toilet and laundry bars, flakes and granules is both interesting and instructive. There are some phases of the explanation of the chemical action of soap with which many chemists may not entirely agree, but these are minor. The authors state that coconut oil is of liquid consistency at "ordinary temperature." This is extremely indefinite, since it and all other members of this group of fixed oils are of the consistency of lard at temperatures of 68 to 70 F and do not become liquid until they are in excess of 80 F.

The next three chapters, which deal with the effects of soap on the normal and on the diseased skin, are, in general, well written. Many dermatologists and pharmacologists, however, will not agree with the statement that the addition of sulfur and mercurials to shampoo mixtures is of decided value.

Chapter V is concerned with the effects of soap on the hair and scalp. It is well done except for a few typographic errors and the use of the word "anti-parasiticide," which occasionally creep into the best of literature.

Chapter VI is poorly written and contains many misstatements and inaccuracies. It also could be improved by some careful editing. In some sections the phraseology is so involved that the material is almost unintelligible, to wit: "in some plants hot water is not provided. No soap will make hot water dispensable nor will hot water make a good soap dispensable. A mediocre soap and hot water are better than a good soap and no hot water. In many areas all water is so hard as to hamper the full action of the soaps described although experience suggests that the heavy-duty soap, as described, almost invariably will suffice in hard water areas." This chapter closes with a brief paragraph, entitled "Summary," which actually summarizes nothing but which is, on the contrary, a conclusion. At one place the author makes the statement that "liquid soaps in order to flow freely through dispensers must be potassium soaps largely made from coconut oil." This is contrary to fact, as with few exceptions, liquid soaps used in dispensers are aqueous solutions of soda soaps, and only sufficient

coconut oil is used in their manufacture to insure optimum lathering properties.

Chapter VII deals with the use of soaps for shaving. Except for several typographic errors, it is well done. Allergists, however, will not agree with the author's trite definition of the phenomenon of allergy as an "abnormal reaction to a specific sensitizing agent." The majority of dermatologists will not agree that shaving is to be recommended for the eradication of nits in pediculosis, regardless of how rapid and how effective the procedure may be. In his discussion of fallacies held by the laity and many members of the medical profession the author states that he was able to shave without irritation because he used magnesia magna as a medium instead of soap, but the real reason is that the former contains only 7 to 8 per cent of magnesium hydroxide in suspension and is very poorly ionized. Soap ionizes readily, and in colloidal suspension in distilled or soft water it maintains a high degree of ionic dissociation.

Chapter VIII deals with cutaneous detergents other than soap and it is excellent. One omission, however, is inexcusable. The reader is given the impression that this type of synthetic detergent is of comparatively recent development. On the contrary, the late Dr. George Henry Fox first introduced this type of substance to the medical profession as long ago as 1890, when he recommended sodium sulfocinoleate for a synthetic detergent as an auxiliary hydrophilic ointment base.

The final chapter, written by the editor, mentions briefly a few of the medical uses of soap, including first aid and hygiene, as a keratolytic agent and others. Too much emphasis is given its use as a prophylactic against venereal disease notwithstanding recent work under the direction of the National Research Council, which has demonstrated its worthlessness as a preventive of syphilis and chancroid.

One illustration, depicting a man with a chancre on the bearded region, bears the legend, "Syphilis a chancre, the primary lesion of syphilis, on the bearded area. Patient used no soap for shaving." What this fact had to do with his getting syphilis, God only knows!

Forty black and white illustrations serve to embellish the text. For no particular reason there is one colored illustration of impetigo contagiosa. Many of the illustrations fail to illustrate anything of particular interest and utilize paper which in these days might better be put to other use.

In conclusion, one may venture the statement that for the dermatologist this book contains some valuable and interesting data. Unfortunately, it contains many misleading statements and considerable evidence that much of it has been carelessly written and edited. The entire edition is being distributed to the medical profession by Proctor and Gamble Company. This may or may not be a commendable procedure.

**Modern Cosmeticology** By Ralph G. Harry, F R I C, Foreword by P B Mumford, M D, F R C P Second edition Price, 35 s Pp 432, with illustrations London Leonard Hill, Ltd, 1944

In his foreword Mumford makes the statement "Perhaps the day will come when the Dermatological

Clinics will enhance their efficiency by accepting the constant help of the physical chemist. 'Modern Cosmeticology' points the way."

In this second edition written for the manufacturing cosmeticologist Harry takes up at some length the pertinent "histology of the skin," "emulsions," "cleansing creams and lotions," "acid creams," "face packs," "vanishing creams," "powder creams," "skin nutrition, skin foods," "astringent lotions," "lip sticks," "face powders," "sunburn preparations," "deodorants and depilatories," "allergy and dermatitis," "antioxidants," "bath preparations," "hand creams," "hair preparations," "manicure preparations," "acne preparations," "chemical examination of cosmetic and toilet preparations" and other subjects. The author is a chemist of some note and writes for the *British Journal of Dermatology*, he reviews a surprising amount of literature, French, German and American as well as English in connection with the discussion of his subject. At one point he even treats at some length of the theory of heredity in relation to baldness. The volume is well illustrated with black and white illustrations and photomicrographs in colors. There are a good index and also pertinent tables in reference to various subjects.

While the book is written for the manufacturing chemist and cosmeticologist, there is much between the covers of interest to the dermatologist. For example, the subject of oil in water and water in oil emulsions is fully discussed.

While the reviewer cannot agree with all the contents, nevertheless, it is a book well worth reading. In fact, the dermatologist may learn much from its contents.

**Penicillin Therapy Including Thyrothricin and Other Antibiotic Therapy.** By John A. Kolmer, M.S., M.D., Dr.P.H., Sc.D., LL.D., L.H.D., F.A.C.P. Price, \$5. Pp. 302. New York: D. Appleton-Century Company, Inc., 1945.

It is a pleasure to review a monograph on penicillin, the discovery of which marks a new era in the proud history of medicine, for not only is penicillin far superior to the sulfonamide compounds in the treatment of infections, but "in the whole realm of chemotherapy no other compound or group of compounds combine such low toxicity with such high therapeutic activity." Still more, penicillin symbolizes to the medical profession and to mankind the unlimited potentialities of medical research with regard to the treatment of disease.

Dr. Kolmer, the author of the monograph, is professor of medicine at Temple University School of Medicine and director of the Research Institute of Cutaneous Medicine. His textbook, "Infection, Immunity and Biologic Therapy," is well known.

This monograph is most timely. Penicillin is being used more and more in the treatment of infections, and a thorough acquaintance with all the aspects of this drug is necessary in order to use it intelligently.

In addition to reporting his own experience with penicillin, the author summarizes the vast amount of important literature which has accumulated since Florey succeeded in isolating penicillin in relatively pure form and in showing its great effectiveness in the treatment of infections in mice. The following topics are dis-

cussed in simple and clearly understandable language: the production of penicillin, the methods for its detection and assay, its physical and chemical properties, its antimicrobial activity in vitro and in vivo, its pharmacology and toxicity and the principles underlying treatment with penicillin of different infections. In addition, the other antibiotic substances are described: thyrothricin, gramicidin, streptothricin, patulin and chlorophyll.

The book contains nineteen tables, enumerating the different infections against which penicillin is effective or ineffective, and illustrations showing particularly the administration of the drug. It is well written and contains some of the most important facts of academic and practical interest regarding penicillin and its use. A large bibliography is given at the end of each chapter. This monograph should be in the possession of every medical practitioner.

**The Hair and Scalp. A Clinical Study (with a Chapter on Hirsuties).** By Agnes Savill, M.A., M.D. (Glasg.), F.R.C.P.I. Third edition. Price, \$4.75. Pp. 304, with 54 illustrations. Baltimore: William Wood & Company, 1945.

This book begins with a chapter on the structure and physiology of the hair, which offers a basic and scientific review of this subject. Following this are two excellent chapters on canities and care of the hair. In the former are listed a number of unique observations on sudden graying of the hair. In the latter there is much sound advice, although the scientific accuracy of the statement, "It is not widely enough known that even dandruff can be conveyed to those who use brushes and combs belonging to individuals whose scalp harbors the malady," is easily challenged. Dr. Savill scientifically describes permanent waving, singeing, bleaching and dyeing of the hair. The fourth chapter, on The Molecular Structure and Elastic Properties of Hair by W. T. Astbury, which includes x-ray diffraction analysis, is an outstanding contribution to the book and should be studied by all physicians interested in the subject.

Dr. Savill's wide experience as a practitioner, gynecologist and dermatologist and her thorough study of the hair over a period of many years have made her descriptions of the numerous dermatoses affecting the scalp and hair concise and authoritative. Her experience as editor of *Savill's Clinical Medicine* has enabled her to include a wealth of practical information in this small volume, especially in regard to the relationship of internal diseases to dermatoses of the scalp and hair.

The format is good. In order to simplify diagnosis and to render the book more useful, the author has arranged the material according to the chief symptom complained of by the patient, followed by a list of its possible causes.

Among the new additions to this third edition are sections on cleansing agents, pigmentation, recent researches on vitamins and endocrine glands, congenital defects, rare tumors of the scalp and others.

This excellent book is recommended unreservedly to the general practitioner, to the specialist and especially to the dermatologist. Dr. Savill has made a fine contribution to the study of the hair and the scalp.

## A NEW CUTANEOUS SYNDROME OCCURRING IN NEW GUINEA AND ADJACENT ISLANDS

### PRELIMINARY REPORT

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While serving for the past two years in the United States Army as a dermatologic consultant in two of its large bases in the Southwest Pacific, I had an excellent opportunity to observe different types of cutaneous diseases occurring in troops living under field conditions in the tropics

My first station was in a base section which included practically all the tropical part of Northern Australia, where a large number of United States troops were concentrated at the time. The headquarters of this base section was an important hospitalization center, receiving not only all patients from organizations in the immediate vicinity but those evacuated from New Guinea.

The type and incidence of disease of the skin seen in the troops and civilians living in that area were approximately the same as would be encountered in similar groups in the United States. There were numerous cases of so-called Barcoo rot or desert sore, but clinical and laboratory study proved them to be identical with ordinary ecthyma.

Shortly after the beginning of the Buna campaign, in the early part of 1943, we began receiving casualties in considerable number from that area, the majority of which were suffering from some form of skin disease. Many presented bizarre types of eruptions which did not fit in with any known classification. The usual picture in these cases was that of a chronic localized or generalized erythematovesicular dermatitis, but there were also numerous cases of severe generalized exfoliative dermatitis of unknown origin and of a peculiar hypertrophic lichenoid eruption unlike anything previously described. This type of eruption (which accounted for probably more than 80 per cent of the total number of patients with dermatologic diseases received from New Guinea) superficially resembled almost every known dermatosis, but even after careful study an accurate diagnosis was often impossible. At that time they were

thought to be atypical forms of such diseases as lichen planus hypertrophicus, infectious eczematoid dermatitis, seborrheic dermatitis, folliculitis, dermatitis venenata, dermatomycosis with "phytids," bacterids, psoriasis, pityriasis rosea, eczema, etc.

As all the patients improved rapidly after their transfer to Australia, where the living conditions were much better than in New Guinea, the high incidence of these diseases and their atypical appearance were attributed to the extreme hardships, unavoidable in jungle warfare, which these men had undergone. Avitaminosis, lowered resistance from malnutrition and a contact dermatitis from some unknown jungle plant were all considered as possible etiologic factors. As the occurrence of superficial pyogenic and mycotic infections is common in soldiers under field conditions, it was thought that the generalized exfoliative and eczematous types might be a sensitization reaction to bacteria or fungi and could be classed as *ids*.

Owing to the fact that these patients were retained only a short time in the base before being evacuated further south, any extensive investigation was impossible at the time. It was not until I was assigned as consultant to another base in New Guinea, where I personally supervised the treatment of several hundred such patients, that I was able to determine that these eruptions which we had previously classified under various diagnoses were in reality a single entity. The concentration of dermatologic patients in this area greatly facilitated the study of this syndrome, so that our knowledge of its symptomatology, etiology and course was greatly increased, and it soon became possible to recognize it early in its course and to differentiate it from other dermatoses.

It should be emphasized at this time that no cases presenting definite evidence of this new entity were observed which did not originate either in New Guinea or on one of the adjacent islands and, further, as far as can be ascertained,

that it did not exist in that area until after its occupation by Allied troops. This was confirmed by Dr. Braun, a graduate of the University of Michigan who had practiced as a medical missionary for the past twelve years in northern New Guinea. As he happened, after his liberation, to be hospitalized in the same hospital where there were a large number of patients with this type of disease I had an opportunity to demonstrate them to him. After seeing them, he stated that he had never observed a similar cutaneous disease in either the natives or the European residents of New Guinea previously.

These eruptions, while not sufficiently characteristic in themselves to identify the disease, generally present certain peculiarities as to type, distribution and course which make a diagnosis possible. These characteristics are (a) tendency to produce pigmented flat or hypertrophic lichenoid lesions sometimes during the course of the disease, (b) production of persistent circumscribed erythematous lesions, (c) characteristic distribution, especially on the external ears and about the eyes, (d) extreme chronicity, (e) decided tendency to severe secondary infection, (f) tendency to progress to a generalized exudative eczematous eruption, especially of the exfoliative type, and (g) peculiar pigmentary change in the lesions, even in the eczematoid type.

#### TYPES

This disease may be divided roughly into three different categories: (1) patchy eczematoid type, (2) hypertrophic lichenoid type, and (3) generalized exfoliative type. All three types may occur in the same patient at some time during the course of the disease, and transition from one form to another is common.

**1 Patchy Eczematoid Type**—This is the most common of the three types and frequently represents an early stage of the hypertrophic lichenoid or exfoliative type, although it may never progress to these stages.

It begins as a small erythematous or erythematovesicular plaque on any part of the body but is most frequently seen on the dorsa of the hands and feet or in the crural region. Other sites of predilection in the order of the frequency of involvement are the ears, eyelids, periorbital regions and conjunctivas and those areas which are often affected in seborrheic dermatitis, e. g., the scalp, eyebrows, lips, bearded region, axillas and pubis.

These early eruptions often so closely resemble a dermatophytosis with phytid, a seborrheic dermatitis or an eczema that an exact clinical diagnosis is difficult. They are extremely recalcitrant

to treatment and slowly spread to the adjacent areas. Their course is generally marked by alternate remission and exacerbation but may be constantly progressive, so that eventually a large part of the skin over the entire body is covered with a weeping, crusted eczematous eruption or a universal exfoliative dermatitis may develop. Impetigenization of the eruption occurs early and may be of a serious nature even in cases that do not progress to a true exfoliative dermatitis. This secondary infection is often out of proportion to the apparently mild eczematous lesions present. An accompanying cellulitis and lymphangitis are frequent, and subsequent infection of the blood stream may occur. On involution the eruption gradually becomes dry and scaly. Not infrequently it progresses to the development of peculiarly pigmented flat or hyperkeratotic lichenoid lesions. These develop on the sites of the former eczematous eruption.

Some patients with this first type of eruption presented definite evidence of photosensitivity with lesions on the backs of the hands and face (and on the dorsa of the feet), while in others no reaction was observed even after prolonged exposure to the sun.

In other patients there occurred what appeared to be a decided primary pyogenic infection. This developed especially in those patients with a seborrheic background. In these the eruption appeared to be sycosis vulgaris, pyoderma of the eyebrows, severe seborrheic dermatitis or widespread folliculitis involving especially the legs. The scalp, pubis and bearded regions were frequently involved. During the later stages of activity and on involution there was often a loss of hair at the sites of the former eczematous lesions, so that a temporary patchy alopecia occurred. This was seen in the loss of hair in a large part of the eyebrow and smaller areas of alopecia in the bearded regions of the upper lip and cheeks. In the scalp the picture was most unusual and unlike any inflammatory alopecia-producing process with which I am familiar. Here the usual picture is a patchy alopecia which apparently starts as a severe inflammatory seborrheic dermatitis of the scalp or as *tinea amiantacea*. At other times a bizarre total marginal alopecia occurs, with a resultant peculiarly shiny wrinkled pseudoatrophic condition of the skin. In this type there is a raised, advancing, circinate, infiltrated border at the edge of the area of alopecia. This border has a brown to gray-brown color. While not all patients were observed until complete regrowth of hair had occurred, I believe that such regrowth is the general rule.

In some of the patients with eczematous manifestations whose eruption was confined to the face and was dry, the disease closely resembled lupus erythematosus, especially when it involved the bulb of the nose and the butterfly regions of the face.

One striking characteristic is the involvement of the external ears. This involvement is frequently pathognomonic and consists of a scaly or erythematovesicular eruption appearing first on the lobes of the ears and later involving the rim of the ear. At times the entire external ear is involved. Unlike the involvement of the eye, there is little if any swelling, which, however, may occur to a moderate degree in the presence of a secondary infection. Involvement of the ears is usually bilateral and may precede for weeks or months any other manifestation of the syndrome. I have seen the later development of hypertrophic lichenoid lesions on the ears, but they are infrequent.

Occasionally small circumscribed circinate persistent erythematous lesions were seen.

It should be emphasized that, while many cases (30 to 40 per cent of all cases) of this purely eczematoid type are seen, frequently the picture is complicated by the development of hyperkeratotic lichenoid lesions and rarely by the development of a generalized exfoliative dermatitis. The latter picture ordinarily develops from those eruptions of the patchy eczematoid type with a widespread or generalized distribution.

*2 Hypertrophic Lichenoid Type* In this form of the disease the eruption so closely resembles that of lichen planus hypertrophicus that it is invariably diagnosed as the latter by any one unfamiliar with the syndrome. In fact, all such cases were so classified by us in the beginning, and it was not until I had an opportunity to observe the development and evolution of a large number of such cases in New Guinea that I came to the conclusion either that I was dealing with a new entity or that the former conception of lichen planus would have to be completely revised.

The eruption in these cases may first appear primarily as small erythematous or violaceous or bluish lichenoid keratotic papules, but more frequently these develop secondarily at the sites of healing eczematous lesions. This eruption is usually distributed on the flexor surfaces of the extremities or about the eyes but may be located on any part of the body. It may spread rapidly, so that a large part of the skin of the entire body is involved in a comparatively short time, or it may slowly extend, new lesions continually appearing on other parts of the body.

Lesions on the eyelids are especially common and to one familiar with the pictures are sufficiently characteristic to make a diagnosis of this syndrome. In the early stages there may occur redness, severe edema with complete closure of one or both eyes and an erysipelas-like appearance. These patients generally have a temperature of 101 to 102 F and are profoundly ill. Under treatment the acute process rapidly subsides, but changes gradually occur in the eyelids and adjacent skin until finally slate-colored infiltration develops on either the upper or the lower eyelid or both. It may sometimes be confined to a bandlike or cordlike infiltration along the edges of the lids.

In other cases the process begins as a subacute inflammatory dermatitis not unlike that due to nail polish. It may be moist or dry, but as it progresses it presents a terminal picture similar to that already described.

In many of these cases with involvement of the eyelids there occur conjunctival injection, keratitis and occasionally ulcers of the cornea. On the scalp slate blue hyperkeratotic inflammatory lesions often develop which appear on the bald patches which have followed eczematous lesions undergoing involution.

Lesions on the mucous membranes of the mouth, the vermilion borders of the lips and the external genitalia (glans and shaft of the penis and the scrotum) are common and, while somewhat similar in appearance to those of lichen planus, are usually much more extensive. In several cases the mucous membrane of the entire mouth was involved, producing a severe stomatitis. Occasionally small bullous lesions were observed.

The type of eruption seen on other parts of the body varies from flat slate-colored pigmented macules which cause no apparent change in the normal texture of the skin to a thick, confluent nodular hyperkeratotic and verrucous form, which is invariably diagnosed hypertrophic lichen planus, even by experienced observers. However, the typical polyangular, flat, violaceous glistening elementary papule of lichen planus is always absent. The lesions may be discrete but are usually confluent, occurring in large patches. The color of the lesions varies from pink to a deep violaceous hue or, at times, when confluent may present a dirty gray-white appearance, somewhat similar to that of an inveterate psoriasis. The eruption is often so extensive that almost all the skin over the entire body is involved. This, together with the peculiar slate-colored pigmentation, gives the patient an extremely bizarre appearance. The pronounced

and peculiar melanoderma is definitely different from that which frequently follows an extensive lichen planus

Lesions on the palms and soles are common and usually consist of slightly scaly, hyperkeratotic large and small papules. At other times the whole palm or skin is thickened and glazed and suggests an ordinary chronic hyperkeratotic eczema

In 2 cases which presented a widespread, severe cystic acne of recent origin, typical pigmented keratotic lichenoid lesions appeared at the sites of involuting follicular lesions and a lichenoid eruption was present on the mucous membranes of the lip and mouth

This lichenoid keratotic type represents about 10 to 15 per cent of the more extensive eruptions seen in patients with this syndrome. However, it should be emphasized that many of these developed from the patchy eczematoid type, although this type may be hyperkeratotic from the beginning. Like those of the first group, in these patients a generalized exfoliative dermatitis may develop

*3 Generalized Exfoliative Type*—Generalized exfoliative dermatitis is of frequent occurrence in this syndrome and usually follows either the patchy eczematoid or the hypertrophic lichenoid type, although it may occur primarily as an erythroderma. If of primary occurrence it is often of the fulminating type with pronounced edema, especially of the face, and with severe constitutional symptoms. In the patchy eczematoid and lichenoid types it may follow the use of injudicious therapy, such as the local application of irritating medicaments. In 2 patients with the hypertrophic lichenoid type of lesions it developed immediately after the use of bismuth subsalicylate intramuscularly. In 1 of these patients a septicemia developed from the secondary infection, and he died

#### CONSTITUTIONAL SYMPTOMS

Many of these patients have relatively mild eruptions which remain more or less stationary over long periods or which may completely disappear if properly treated. However, a slow progression or recurrence of the disease is the rule, so that the patient eventually requires hospitalization and subsequent evacuation from the theater. It was the latter group which formed the basis for the present study

In most of the hospitalized patients there were loss of weight, fatigue and inability to perform any duty. In some a rise of temperature and other evidence of a profound toxemia were present

The blood picture, aside from a mild eosinophilia in some cases and a leukocytosis in those in which secondary infection was present, remained essentially normal. In 2 cases profound changes occurred which will be discussed in a later paper

#### COURSE OF THE DISEASE

As previously stated, the course of this disease is characterized by periods of remission and exacerbation, and complete recovery rarely or never takes place as long as the patient remains in the New Guinea area. For that reason, all persons showing definite manifestations of this syndrome are evacuated to a temperate climate as soon as practicable. On account of these circumstances, it was impossible to make accurate observations as to the final outcome in cases of the severer types of the disease

However, I did have an opportunity to watch the progress of 150 such patients for twenty-one days during their return voyage to the United States. Approximately 20 per cent of them were litter patients with the severe generalized type, the others being ambulatory patients with a comparatively mild form of the disease, mostly of the patchy eczematoid type. All of these patients improved greatly, although the living conditions aboard ship were mediocre and the weather extremely warm during most of the voyage. Also, during a short trip recently to the mainland of Australia I was able to visit an Australian army hospital which treats practically all dermatologic patients evacuated by the Australian army from the advanced areas. Major Foote, the dermatologist in charge, showed me a large number of patients who presented the typical picture of this syndrome and in all of whom it had developed while they were either in New Guinea or on the adjacent islands. He stated that, judging by his experience in treating these patients for over two years, their average length of hospitalization after they returned to Australia was approximately three months. He also stated that the majority, even those with the most severe type, recovered completely in this length of time

#### ETIOLOGY, PATHOGENESIS AND TREATMENT

Since this communication is in the nature of a preliminary report, etiology, pathogenesis and treatment of this syndrome will be discussed in a later paper. However, on the basis of my experience, it would seem advisable that only the mildest topical remedies be employed and, further, that the sulfonamide compounds and

other preparations used for lichen planus are contraindicated. Penicillin has completely revolutionized the treatment of the severe generalized exfoliative and eczematoid forms of this disease, in which secondary infection with grave results often occurs. Instead of waiting, as we had previously done, until serious complications such as septicemia or pneumonia occurred, we now give this drug immediately to all patients in whom any considerable amount of infection develops. The results are so spectacular that we at first thought that penicillin might have some actual detoxifying effect on the disease itself. In a few hours the patient's general condition becomes much improved, the temperature drops and the secondary infection of skin rapidly clears, so that instead of a weeping, crusted pyoderma there is an erythematous smooth surface with little evidence of inflammatory change. One of the great advantages of this type of treatment has been the great reduction in the amount of nursing care as compared with that formerly required for patients with this type of disease. The use of the usual prolonged tub baths and extensive, continuous wet dressing are unnecessary, and the patient requires no more special nursing or medical care than a patient with ordinary generalized eczema. The patients are

given 150,000 units of penicillin in the first twenty-four hours and 80,000 units daily thereafter as a maintenance dose. In no patients so treated have any serious complications occurred.

NOTE—This article was prepared at a time when it was considered inadvisable to mention quinacrine hydrochloride as the etiologic agent on account of the possible adverse effect such a statement might have on the malaria control program used in the Pacific Theater of War by both the Army and the Navy.<sup>1</sup> From the beginning, when I first observed the lichenoid and exfoliative types of this disease, there was no question in my mind regarding the role of quinacrine in that particular type. However, it was not until after I had the opportunity to observe the transition of the eczematoid type to the lichenoid type in the early part of 1944 that I was able to determine that they were the same disease. My conclusions on this subject were transmitted to the proper authorities in a letter dated June 15, 1944 and in other subsequent reports. Since this article was written much additional information has been obtained which, in my opinion, definitely incriminates quinacrine as the etiologic agent involved in this unique dermatitis.

Another communication is being prepared incorporating these data, which will be submitted for publication in the near future.

1 This report was first submitted to the Army Medical Department in November 1944. It was not released by the War Department for publication until the conclusion of the war with Japan.



# CLINICAL INVESTIGATION OF A NEW CUTANEOUS ENTITY

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AND

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MEDICAL CORPS, AUSTRALIAN ARMY

We wish to call attention to an unusual eruption which occurred among the military personnel in the Southwest Pacific area. The affected persons were members of the Australian and American forces whose stay in the tropics ranged from two to sixteen months.

The first patient was seen in October 1943. The number seen by us has steadily increased to 47 at the time of this writing. Some patients have been under constant observation and study, others were observed for only relatively short periods. New cases are still developing, and the study is continuing. Many physicians in the Southwest Pacific area have cooperated by exchanging information and by allowing us to observe patients who presented the eruption on which we are reporting.

The syndrome invariably began with an initial eruption which varied widely in different persons. This early eruption mimicked such common dermatoses as heat rash, fungus infection, eczema, urticaria and contact dermatitis. After the initial picture there followed characteristic firm violaceous elevated papules, nodules or plaques, which in some cases remained mild and localized and were of no serious consequence while in other cases the involvement was severe and widespread and at times was accompanied with a potentially fatal acute exfoliative dermatitis.

That the eruption has puzzled many experienced dermatologists is evidenced by the many widely varying diagnoses they have given it. Not until the same syndrome was repeated in increasing numbers of patients did we realize that we were dealing with a new entity. We were unable to find any reports of a similar syndrome recorded in the literature.

## INITIAL ERUPTION

The initial eruption consisted of a wide variety of cutaneous lesions, none of which had any

This report was first submitted to the Army Medical Department in June 1944. It was not released by the War Department for publication until the conclusion of the war with Japan.

definite diagnostic features. The beginning eruption might be (1) round or irregular superficial scaly patches, resembling a fungus infection, (2) discrete and confluent pink or red pinhead-sized vesicles and papules, like *miliaria*, (3) variously sized round or elongated skin-colored or slightly erythematous elevated lesions which were weltlike but neither pruritic nor evanescent, (4) simple erythematous patches which soon became scaly and progressed to an exfoliating dermatitis, and (5) variants of the preceding. For example, the elevated nodules became punched-out ulcers, the scaly patches became infiltrated and fissured as an eczema, or the

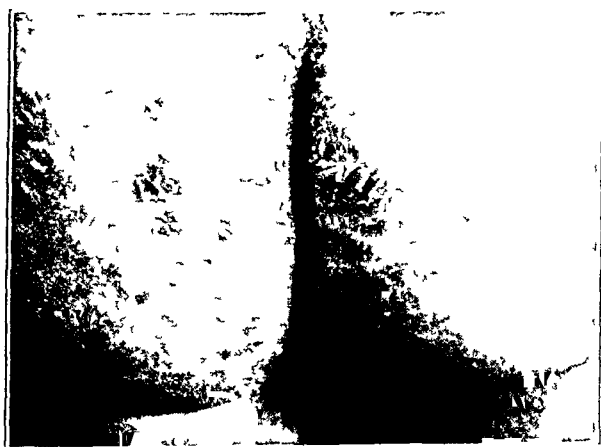


Fig 1—Scale-covered papules of two weeks' duration

vesicles were associated with bullae and gave the appearance of a contact dermatitis.

The hands, including the palms, the axillae, the soles and the groins were the sites most commonly affected.

## SECONDARY OR CHARACTERISTIC LESIONS

From two to eight weeks after the onset of the primary eruption, there appeared bilateral and roughly symmetric elevated, firm, rounded or elongated, violaceous papules and nodules which ranged in size from 0.8 to 4 cm. At first these lesions were soft and smooth surfaced, later they became leathery and verrucous.

The large elevated papules and nodules began as such and were never the result of coalescence of small papules. Widely separated groups or patches of violaceous papules with an occasional verrucous nodule comprised the entire picture in the patients with milder eruptions. In addition to papules, many nodules and plateau-like



Fig 2—Characteristic elevated, infiltrated papules of three months' duration

elevated patches with the same violaceous color and leathery surfaces also occurred. We termed these verrucous plaques.

At times, the original presenting eruption was entirely replaced by the characteristic nodules, in other instances, the original eruption persisted and even progressed. For example, the superficial scaly fungus-like patches in some cases increased by peripheral extension and formed an extensive background for the nodules. The wheal-like early manifestation sometimes progressed to form typical characteristic purplish nodules which comprised the entire secondary picture, the surrounding skin being entirely normal. In some cases there was an accompanying localized erythroderma which gave the surrounding skin a deep red or magenta color. In other patients, with more severe eruptions, an acute exfoliative dermatitis occurred. It began at a period between the primary eruption and the development of the characteristic nodules or simultaneously with the development of the nodules. In 2 cases, the elevated lesions rapidly became denuded and developed into punched-out ulcers, which soon became infected and resembled a pyoderma.

Deeply violaceous pea-sized sessile warty excrescences, having a predilection for the inner surfaces of the thighs and the suprapubic regions, were present in the patients with more serious involvement. Patches of minute acuminate follicular papules or filiform spines were at times distributed independently of the papules and nodules.

The covered parts of the body were involved more frequently than the exposed areas. The waistline, suprapubic region, intergluteal fold, hands, eyelids, groins, axillary folds, helixes of the ears, shaft of the penis, scrotum, arms, feet, legs, chest and back were involved in frequency about in the order named. At times there was a tendency for the lesions to occur over sites of pressure. The upper eyelids were almost constantly affected, while the remainder of the face was rarely involved.

#### LESIONS OF THE MUCOUS MEMBRANES

Approximately one third of the patients presented discrete and confluent, tense, grayish white papules on the lower lip and reticulated, streaked,



Fig 3—Verrucous nodules and plaques of six months' duration

firm, grayish white patches on the buccal mucosa and the lateral and dorsal surfaces of the tongue. Four patients had elevated, irregular, ulcerated, hypertrophic tumefactions on the buccal mucosa and lateral margins of the tongue. Careful

search revealed no papules on the glans penis in any case. Superficial scaly patches were seen about the meatus in 2 cases. The latter type of rash was commonly found on the scrotum and on 2 occasions involved the mucous membrane of the prepuce. The mucosa of the anus was involved by scaly, slightly infiltrated plaques in 4 cases.

#### SYMPTOMS

No subjective symptoms were associated with the beginning of the eruption. As the primary eruption progressed, moderate to severe pruritus was common. This itching continued until after the characteristic elevated secondary lesions were well established, after which time it gradually diminished. Soreness of the tongue and cheeks occurred when ulcerated lesions were present. The patients with involvement of the anal mucosa complained of pain on defecation. Fissuring of the intergluteal fold frequently caused pain or discomfort. Constitutional symptoms were present only in those persons who exhibited widespread erythroderma or generalized exfoliative dermatitis. Slight to moderate fever, chills, debility, tenderness and stiffness of the skin, anorexia and intractable itching were the usual complaints. Hypertrophy of lymph nodes, sufficiently severe to cause discomfort and pain, was observed; the inguinal lymph nodes were chiefly involved. Decubitus ulcers occurred in the region of the hips in 1 case.

#### SEQUELAE

Our observations and study extend over a period of seven months, but included among the subjects were some whose eruption began almost a year before. Changes are still occurring in these patients, and consequently the true story of the final stage is not known.

*A Pigmentary Dystrophy*—In the patients with milder eruptions a localized patchy blue to gray-blue pigmentation persisted after the elevated papules and nodules had disappeared. In some with mild eruptions the papules resolved, leaving depigmented macules. A generalized reticulated and solid grayish blue and tan rust staining appeared in the persons with severe eruptions.

These patients when viewed from a distance presented a picture of diffuse total staining like argyria that had missed the face. Closer examination showed that the staining was composed of many colors and was solid in some areas and mottled in others. The color slowly became less intense as the months went by and areas approaching normal skin could be seen, but the rate of improvement was exceedingly slow.

Deeply pigmented, negroid, pinhead-sized to pea-sized macular patches were frequently seen on the posterior surfaces of the neck and shoulders. These pigmented patches were not sites of previous papules or nodules.

*B Cutaneous Atrophy*—In the patients with severe eruptions a reticulated cutaneous atrophy occurred at the site of the papules, nodules and plaques after their disappearance. In the same patients, however, the atrophy on the hands was confluent and resulted in a dry, thin, wrinkled skin. This picture existed to a less degree on the feet. The color of the hands changed to a livid



Fig 4—Generalized pigmentation in a patient with a severe eruption. The face and the center of the back were the only unaffected areas. The duration was eleven months.

blue when they were placed in a dependent position. This atrophy was not unlike acrodermatitis chronica atrophicans or poikiloderma atrophicans vasculare. No telangiectasia was present.

*C Alopecia*—Wherever an infiltrated plaque or elevated nodule occurred on the body, partial or complete loss of hair resulted. A patchy alopecia of the occipital region was present in most cases. Two patients suffered total loss of hair.

*D Involvement of Nails* The 2 patients who had alopecia totalis lost all their nails. Some lost only a few nails. The toe nails were seldom affected. When erythroderma occurred on the extremities, paronychia involvement usually took place and was invariably followed by disturbances of the nails in the form of deep cross ridging or tremendous piling up of the nail substance, with loosening of the nail plate.

*E Disturbances of Sweat Glands and Sebaceous Glands*—An almost complete loss of function of the sweat glands resulted when the disease was severe. This was accompanied with a diminished function of the sebaceous glands. During a follow-up examination we observed patients perspiring profusely in unaffected areas, such as the face,



Fig 5—Pigmentation and cutaneous atrophy of the feet

and at the same time the rest of the body, including the axillae, palms and soles, were powder dry. The scalp usually showed a decreased production of oil. Several patients later volunteered the information that slight sweating returned to previously dry areas, such as the palms. No disturbance of function of sweat glands or oil glands existed in the patients with milder disease.

#### LABORATORY OBSERVATIONS

Laboratory investigation included urinalyses, blood cultures, icterus index determinations, sugar tolerance tests, serologic tests for syphilis, direct examinations and cultures of scales for fungi. All these tests failed to reveal anything abnormal. The only observation of significance

was the presence of malarial parasites in about one third of the patients.

Infiltrated papules or nodules were excised for microscopic study in the majority of cases. Representative case sections were studied by Major Mark Bracken, a pathologist, who gave this report: "The sections are remarkably constant in their morphologic pathologic changes. The degree of hyperkeratosis varies somewhat, but acanthosis and the thickening of the stratum granulosum are similar in all sections. Rete pegs are elongated, and papillae are widened and contain moderately dilated capillaries. Numerous chromatophores containing a brown, coarsely granular pigment are present at the apex of the papillae and can also be seen in the epidermis to a less degree. The inflammatory reaction is practically confined to the superficial portion of the corium, so that there is a line of demarcation separating the superficial and the deeper layers of the corium. This inflammatory reaction is diffuse and is composed of round cells (both lymphocytes and plasma cells), a few neutrophils and a moderate number of eosinophils. In areas where the inflammation is present in the deeper part of the corium, it can be seen only around the sweat glands and capillaries."

#### ETIOLOGY

When the same unusual cutaneous syndrome was repeated in different persons from the Australian and the United States armies, we became suspicious that we were seeing a new entity. Our first step in analyzing the problem was to determine what factor or factors were common to every case. Every affected person had been in tropical service but from widely different areas. After many possible agents and elements were carefully considered and eliminated, there remained only one constant factor and that was quinacrine hydrochloride.

Since these patients were from malarious zones, they were required to take quinacrine for prophylactic or suppressive malarial treatment. In not a single instance did the eruption occur in a person who had not taken quinacrine hydrochloride. We deduced that it was possible that the drug, either alone or in combination with other factors, produced this peculiar eruption. Then it was decided to prove this in the same manner that other drug eruptions have been proved—that is, by observing whether the eruption disappeared when administration of the drug was discontinued and reappeared when it was again administered.

After quinacrine was withdrawn, the eruption progressed for a short time and then remained stationary for a variable period. During this

period no new lesions appeared and the existing ones remained unchanged. In the persons with milder eruptions, improvement commenced two to four weeks after they stopped taking the drug. The more severely affected persons required four to eight weeks before evidence of regression could be seen. This arrested activity of the process and subsequent progressive improvement occurred in every case after use of quinacrine was discontinued, regardless of the treatment used.

Nine patients who had complete or almost complete clearance were again given the drug. In 4, whose eruptions had been classified as severe, new characteristic violaceous papules reappeared in three to fourteen days. Two patients had a return of their exfoliative dermatitis when quinacrine was readministered. Three persons with moderate involvement did not have a re-appearance of characteristic violaceous papules at the time of this writing, which was two weeks after the drug had been readministered. However, they did have mildly erythematous patches which may precede the infiltrated papules.

In the early treatment of the initial eruption, irritating ointments containing sulfur or salicylic acid were frequently used. This often resulted in the rapid and widespread appearance of the characteristic violaceous papules and nodules. This was confusing when we were considering the possible etiologic agents. We now believe that this treatment acted as a precipitating factor to the actual causative agent.

#### INCIDENCE

Although many thousands of persons have taken quinacrine hydrochloride over relatively long periods, the number showing intolerance to the drug as evidenced by cutaneous manifestations was extremely small.

#### TREATMENT

As soon as quinacrine hydrochloride was suspected as the causative agent, its use was discontinued. If the patient required malarial therapy, quinine was used. In the earliest phase of the syndrome, antipruritics, such as calamine lotion and dusting powders, were indicated. The early eruption was often aggravated or camouflaged by a contact dermatitis caused by the application of such medicaments as ointment of benzoic and salicylic acid N F, Castellani's paint, sulfur ointment and sulfonamide ointments.

For the advanced eruptions which were associated with localized erythroderma or acute exfoliative dermatitis, soothing baths containing bran, starch or sodium bicarbonate were used. Calamine lotion and zinc oxide paste used after the bath had a soothing effect.

Several patients with severe lesions improved considerably on this regimen although the offending drug had not been withdrawn. However, the improvement occurred only in the acute inflammatory process, there was no regression of the infiltrated plaques and nodules. On the contrary, these lesions progressed and new ones appeared.

Intravenous injections of sodium thiosulfate did not influence the normal regression of the nodules. In 2 instances, arsenic in the form of solution of potassium arsenite seemed to expedite the disappearance of elevated nodules and papules. In many others, the same drug, as well as parenterally administered arsenicals, did not influence the rate of clearing. Improvement occurred constantly in two to eight weeks after withdrawal of quinacrine hydrochloride with or without treatment. The elevated nodules usually required two to six months to disappear, while the warty excrescences persisted more than eleven months. The lesions of the mucous membranes were among the first to regress.

#### DIFFERENTIAL DIAGNOSIS

*A Primary Eruption*—The primary eruption has been confused with fungus infection, heat rash, urticaria, pityriasis rosea, psoriasis, contact dermatitis and scabies.

1 Fungus Infection. No spores or hyphae were found on direct examination of scales. No fungus grew on attempted culture.

2 Heat Rash or Lichen Tropicus. The appearance was so similar that differentiation was not possible.

3 Urticaria. The persistence of the lesions and the variability of itching were important distinguishing features.

4 Pityriasis Rosea. At first, differentiation was not possible. Later, the persistence of the scaly patches and the involvement of the feet and ankles were helpful.

5 Psoriasis. The scaling was furfuraceous and unlike the heavy silvery scaling of psoriasis. No pinpoint bleeding appeared after removal of scales. The elbows and knees were not so commonly involved as in psoriasis.

6 Contact Dermatitis. The tendency of involvement about the groins, waist and axillas suggested contact dermatitis, possibly from clothing. Lack of facial involvement was against the diagnosis of ordinary dermatitis venenata. A true contact dermatitis due to sulfur, salicylic acid and sulfonamide ointments at times complicated the picture.

*B Secondary Eruption*—The secondary eruption had to be distinguished from aberrant forms

of lichen planus, infectious eczematoid dermatitis, prurigo nodularis, mycosis fungoides, nodular leprosy, syphilis and lymphoblastoma

1 *Abeirant Forms of Lichen Planus* Lichen planus hypertrophicus and lichen planus verrucosus, unusual types of lichen planus, begin as typical glistening polygonal papules which later coalesce. Often satellite papules persist. A history of typical papules was never present, nor were such papules ever seen by us. The hypertrophic nodules and plaques were the result of direct extension of a beginning papule or nodule and not the consequence of fusion of papules. The verrucous plaques did not have a predilection for the legs. These rare forms of lichen planus are usually chronic and remain unchanged for years. The nodules and plaques in our series of patients regularly showed improvement in approximately eight weeks after withdrawal of quinacrine hydrochloride, regardless of other treatment. Such regular and uniform improvement in every case in a relatively short time is inconsistent with our experience and that of other dermatologists who have observed cases of atypical lichen planus. This same experience has shown that lesions of the mucous membranes in lichen planus are most recalcitrant to therapy and in the exceptional case in which they improve or clear it is always long after the skin has shown improvement.

2 *Infectious Eczematoid Dermatitis* When the surfaces of the nodules became denuded, secondary infection with crusting and exudation occurred. Before the development of the typical violaceous color, differential diagnosis was extremely difficult. The eruption had the appearance of widespread deep-seated pyoderma.

3 *Prurigo Nodularis, or Lichen Obtusus* In prurigo nodularis, the nodules are skin colored or red and are most often confined to the arms and legs. The nodules we are describing had a violaceous color and were never limited to the extremities. In addition, the pruritus of our patients was not as intense as of patients with prurigo nodularis, and the onset was more rapid.

4 *Mycosis Fungoides* Before the appearance of characteristic purplish nodules, the differential diagnosis in some cases was impossible. Microscopic examination of sections would readily differentiate the two diseases.

5 *Lepromatous Leprosy* No constitutional symptoms preceded the eruption of the nodules. There was never any evidence of the yellow glossy appearance seen in lepromatous leprosy. Again, laboratory procedures would be diagnostic, for a nasal smear when rhinitis is present should yield Hansen's bacilli and microscopic

section of a nodule would reveal characteristic foam cells.

6 *Syphilis* There was a striking resemblance to a papular syphiloderm in a few cases. In others, the eruption could have been confused with nodular tertiary lesions except that the color of the nodules in syphilis should be dull red and not violaceous. Serologic tests for syphilis should be helpful.

7 *Lymphoblastoma* Leukemia cutis and Hodgkin's disease might readily be confused with this eruption. The absence of constitutional signs and symptoms is important. Hematologic study should rule out leukemia, and microscopic examination of sections would readily differentiate these diseases.

8 *Acanthosis Nigricans* The pea-sized, heavily pigmented warty excrescences present in patients with severe eruptions had the appearance of acanthosis nigricans lesions of similar size and shape. Constitutional symptoms, such as asthenia, were not present. Associated indurated nodules are not found in acanthosis nigricans. Microscopic study would show the absence of cellular infiltrate in the cutis.

*C Eruptions of Mucous Membranes* The lesions which occurred on the buccal mucosa, tongue and lips had a great similarity to lichen planus or leukoplakia. One patient was evacuated to a general hospital for roentgenologic treatment of "leukoplakia" involving the buccal mucosa.

1 *Lichen Planus* The papules and striated grayish white plaques which occurred on the lips and buccal mucosa were in no way different from those of lichen planus. However, lichen planus of the tongue and buccal mucosa rarely becomes hypertrophic and ulcerative.

2 *Leukoplakia* Leukoplakia is more insidious in onset, and ulceration takes place after infiltrated whitish plaques have been present a long time.

#### REPORT OF CASES

The following reports represent some of the types of onset and illustrate the disease in various degrees of severity. In each case, suppressive or prophylactic treatment with quinacrine hydrochloride was commenced either shortly before or immediately on the patient's entering tropical service, unless otherwise noted.

CASE 1—A white American officer, aged 38, began tropical service in September 1943. Two months later, an eruption composed of pinpoint vesicles appeared under a finger ring on his left hand. About three weeks later, similar lesions occurred on the left foot in the region of the first interspace. Castellani's paint was applied daily and at first improved the eruption but later irritated it. Within a few weeks, the right hand and right foot became involved, and potassium perman-

ganate soaks and later boric acid soaks were used. In March 1944, four roentgen ray treatments caused apparent improvement. During all this period, he continued his duties without interruption. On March 23, while on his way to a leave area, both hands suddenly became much worse. This exacerbation soon affected the feet, and a similar eruption occurred on the upper eyelids, scalp, arms and shaft of the penis.

On April 3, he was admitted to the One Hundred and Eighteenth American General Hospital, where the areas already noted as involved were seen to present erythematous, slightly scaly papules which were grouped and for the most part confluent. The hands and feet showed few violaceous papules, and the eruption consisted chiefly of a low grade dermatitis. General physical examination revealed nothing abnormal except the conditions noted.

Results of all laboratory procedures, including a complete blood count, and urinalyses were normal, and serologic tests for syphilis elicited negative reactions.

Boric acid compresses and soaks were used for all the areas involved, and the inflammation receded immediately. He discontinued the use of quinacrine hydrochloride on April 17 (two weeks after entering the hospital). About the same time, violaceous, elevated patches appeared on the eyelids, scalp, hands, shaft of the penis, glans penis and arms. These infiltrated patches were composed of ill defined papules. On May 4 (one month after hospitalization) moderately depigmented patches were present in all the formerly involved areas and a few violaceous patches persisted.

When questioned later, the patient revealed that he had symptoms of malaria in early November 1943 and at that time increased the dose of quinacrine hydrochloride to 0.3 Gm daily for two weeks and then continued with 0.2 Gm daily.

**CASE 2**—A white American soldier, aged 36, began tropical service on May 15, 1943. He was well until five months later (October), when moderately itchy "skin-colored and red welts" appeared on the inner surfaces of the left thigh. After a few days, flat red scaly patches appeared on the corresponding area of the opposite side. The eruption spread slowly and did not interfere with the performance of his duties. In approximately three months, the arms, lower part of the abdomen, buttocks and penis were involved by scaly lesions. Additional "welts" appeared on the left cubital area and in the suprapubic region. He was admitted to a field hospital on Jan. 27, 1944 and remained there for approximately one month. According to the patient, a diagnosis of ringworm was made and tincture of iodine and alcohol were applied. New lesions appeared, the older ones extended, and none regressed. He then spent three weeks in a station hospital, where he became worse. While there, he received two intramuscular injections of a bismuth preparation, and various ointments were applied to the eruptions, which had become more pruritic. On March 20, he was sent to the One Hundred and Eighteenth General Hospital with these diagnoses: (1) "acute unclassified dermatitis," (2) lichen planus of wrists, thighs, clavicular regions, cubital spaces and lower part of the abdomen. Moderately severe lesions were present in the mouth.

Examination at that time showed elongated, slightly scaly, papular patches on both upper eyelids, the rest of the face was uninvolved. The lower half of the chest and the upper part of the abdomen were covered with gyrate scale-covered red and violaceous flat patches. Within these patches were isolated discrete and confluent pea-sized to bean-sized similarly colored elevated

papules and nodules. The supraclavicular areas, suprapubic region and inner surfaces of the thighs presented groups of these elevated lesions. The last-named location contained five closely set nodules or tumors. The largest measured 3 by 5 cm and was elevated 1 cm above the normal skin. These larger nodules were dry and leathery or verrucous, some were covered with a fine gray scale. The legs, flexures of the arms and dorsal surfaces of the feet showed the same scale covered gyrate patches, but few elevated nodules were present. Many grouped, infiltrated, scaly patches were seen on the scrotum and shaft of the penis. The glans penis was unaffected. Posteriorly, the lower part of the back and the buttocks, thighs, legs and perianal region presented the same gyrate eruption. The scalp was not involved. White, slightly elevated, striated patches were present on the inner surfaces of both cheeks, while the tongue and lips were normal.



Fig. 6 (case 2)—Close-up view of verrucous nodules and tumors of the inner surface of a thigh.

Physical examination revealed a well developed soldier who did not appear ill and whose only complaint was itching. His temperature was 97.6 F, respiration rate 20 and blood pressure 130 systolic and 80 diastolic. Except for the involvement of the skin and mucous membranes, there were no abnormal physical conditions. There was no history of allergy in the patient or his family. He had not been ill prior to the onset of his present trouble, and no signs or symptoms of malaria had been manifested. The only history of previous trouble with the skin was "athlete's foot" eight months previously.

Results of laboratory studies, including a complete blood count, urinalyses and van den Bergh test for bilirubin were all within normal limits. Serologic tests for syphilis elicited negative reactions. Examinations of scrapings of skin for fungi and of the blood for malarial parasites were unsuccessful.



Use of quinacrine was discontinued on March 20, but new lesions continued to appear for approximately two weeks. During the following two weeks, the eruption continued practically unchanged. On April 18, a decrease in size of the papules located on the eyelids was noted. Within a few days the violaceous tumors and nodules became soft or doughy and the oral lesions were almost imperceptible. Six weeks after the discontinuance of the drug, the papules had disappeared from the upper lids and only a pale brown mottled pigmentation remained. No lesions were present on the lips or within the mouth. All the elevated lesions were flatter, and the color was dull violaceous. Almost encasing the lower part of the chest and the upper part of the abdomen were large, irregular, smooth, glistening, homogeneous pale pink patches. A scale-covered slightly elevated red border approximately 0.2 cm in width margined some areas, while other parts had an ill defined margin. The suprapubic area, the flexor surfaces of the forearms and the anterior surfaces of the thighs and legs presented similar, but smaller, patches. Several irregular scaly lichenified plaques were present within the larger pink-stained areas on the flexor surfaces of the forearms. Four faded violaceous nodules were seen in the lower part of the abdomen. A large elongated papule was located on the dorsum of the penis, and the glans was free of lesions. The large nodules and tumors on the inner surfaces of the thighs were much softer and flatter, and the purplish color was faded. Posteriorly, the arms, lower part of the back, thighs and buttocks showed the same pink or dusky red staining. A fissure had occurred in the inner gluteal fold, but anal involvement was not present.

By May 28, approximately two months after use of quinacrine had been discontinued, a progressive improvement had taken place. Only the larger, more infiltrated papules persisted, these had flattened and faded considerably. The former glistening patches had cleared and were replaced by a superficial confluent atrophy.

CASE 3—A 27 year old white American private began duty in New Guinea on Feb 15, 1943. He was well until Jan 15, 1944, when dark red, intensely itchy variously sized flat patches occurred on the backs of his hands and fingers, the flexures of the wrists and the buttocks. Within a week, the popliteal spaces, knees and dorsal surfaces of the feet were involved. He noted that the eruption was always bilateral and almost symmetric. The intense itching was aggravated by perspiration and heat.

On January 31, he was admitted to an evacuation hospital, where he was treated for "ringworm" with "a red dye." He improved sufficiently to return to duty in two weeks. Two days after discharge, he was again hospitalized, because the eruption was worse and was intensely itchy. The red dye was again used, but the eruption progressed rapidly. On February 16, he was transferred to a station hospital, where he received injections of a bismuth preparation intramuscularly and application of a phenol-containing ointment locally. The eruption had spread to the cubital area of the arms, elbows, axillas, groins, abdomen, inner side of the thighs, middle of the chest "under identification tags," shoulders, upper and lower eyelids, neck, posterior scalp, ears and ventral surfaces of the penis. While he was in this hospital, the following note was made on February 17: "The patient has itchy, raised, patchy, red to violaceous lesions on both feet wrists, flexor surfaces of forearms and axillas. The lesions are rather irregular in outline and not distinctly demarcated. No lesions are seen in the mouth."

On March 20, he was transferred to this general hospital. He did not appear ill and complained only of severe itching. His temperature was 98.4 F, pulse rate 72, respiration rate 18 and blood pressure 130 systolic and 80 diastolic. He stated that he had had no serious illness or hospitalization prior to his present trouble. No personal or family history of sensitivity to drugs or other allergy was obtained. He had discontinued use of quinacrine on February 10, and no malarial symptoms had occurred.

General physical examination revealed nothing abnormal or unusual. His eruption involved the eyelids, chin, tip of the nose, neck, posterior scalp, axillas and axillary folds, elbows, cubital spaces, flexures of wrists, backs of hands and fingers, lower part of the abdomen, groins, inner surfaces of thighs, buttocks, knees, popliteal spaces, legs, dorsum of feet and toes, and ventral surface of the shaft of the penis. The lesions consisted of violaceous papules and slightly elevated plaques which varied in diameter from 1 to 3 cm. Some lesions were covered by a fine scale. Multiple gray-white striations were present on the inner surfaces of both cheeks.

Laboratory procedures, including a complete blood count and urinalyses, van den Bergh test and study of a blood film for malarial parasites, showed normal conditions, and serologic tests for syphilis elicited negative reactions.

The treatment consisted of use of solution of potassium arsenite in increasing doses and a bland ointment for relief of itching. New, less violaceous lesions appeared on the sides of the neck and the right temple. The older lesions became more elevated, especially on the feet and ankles. On April 13, or approximately two months after he had discontinued taking quinacrine, the elevated lesions were flatter and the color had faded to a mottled instead of a deep purple. No scaling was present. On April 18, three small isolated bullae occurred in the infiltrated or thickened plaques. A sparseness of hair was noted in the suprapubic, anal and occipital regions. Numerous patches of filiform keratotic spines were present over most of the body.

CASE 4—A white American officer, aged 36, had been stationed in New Guinea four months when he began to have trouble with his skin. On Nov 1, 1943, he reported for treatment of a dry, superficial, scaly eruption in his axillas and groins. A diagnosis of "ringworm" was made, and calamine lotion containing sulfur was prescribed. Two days later, scaly, pruritic, skin-colored "welts" abruptly appeared on the backs of his hands. About the same time, similar elevated lesions occurred on his neck and chest, under the identification tags and neck chain. The character of the eruption changed rapidly, for within two days the elevated areas were dark red and scaly and within four days they were denuded and oozed a thin clear serum. The patient stated that the pressure and friction of heavy clothing required by his duty were partly responsible for the denudation. He observed that the wearing of heavy socks and shoes had the same effect on the "welts" which occurred two days later on the feet.

By March 14, 1944, the involvement was so widespread that he was hospitalized. He was not acutely ill and complained only of mild itching. All the elevated "welts" were now inflamed and raw and covered with pus and crusts. The attending physician stated that the secondary infection was the chief concern of the moment. He prescribed sulfadiazine by mouth and calamine lotion containing sulfadiazine. Moist compresses were ordered as local applications. Fungicidal agents were applied to his axillas, groins and feet. While in this hospital, many new "welts" made their appearance. The entire

lower lip became swollen and ulcerated and covered with a dark red incrustation. On March 27, he was transferred to a field hospital, with the diagnosis of "subacute infectious eczematoid dermatitis."

His condition became progressively worse, and on March 31 he was transferred to the One Hundred and Eighteenth General Hospital. Although he had had no local treatment for four days, he complained of little discomfort and had no constitutional symptoms. Pledgets of cotton had been placed on every raw area to protect the clothing from the oozing serum. After the adherent cotton had been soaked off, many variously sized punched-out moist ulcers were seen on every part of the body except the face and scalp. These ulcers varied from 2 to 4 cm in diameter and were grouped in the following locations: about the neck in necklace fashion, in the center of the chest, on the posterior surfaces of the thighs, along the waist line posteriorly, on the feet and on both palmar and dorsal surfaces of the hands. Except for a moderate erythema surrounding each ulcer, the skin between the lesions was unaffected. Erythema and tender swelling were present about the cuticle of all fingers, and yellow pus was readily expressed from beneath the cuticle. A moist, meaty red ulcer, approximately 2.5 cm in diameter, involved the margin of the right thumb. A similar type of ulceration covered the entire lower lip. Grayish white striations of patchy distribution were seen on the dorsum of the tongue and on the left buccal mucosa. General physical examination revealed no abnormal conditions except those already described on the skin and in the mouth.

Warm sodium bicarbonate baths for one hour twice daily were started, and calamine lotion was applied between baths. Later, zinc oxide paste was substituted for the calamine lotion. After one week the ulcers were clean and the surrounding inflammation had subsided. The inflammations about the fingers improved to such an extent that the previous tenderness and stiffness had vanished. In about two weeks, practically all the ulcers healed, and the site of each ulcer slowly became transformed into an elevated violaceous papule or nodule. While this was occurring, new firm non-ulcerated, violaceous nodules appeared elsewhere.

Laboratory procedures, including a complete blood count, urinalyses and study of blood for malaria revealed normal conditions, and serologic tests for syphilis elicited negative reactions.

On April 17, four weeks after he entered the hospital, use of quinacrine was discontinued. Leathery verrucous violaceous nodules were now present for the first time. The ulceration of the lower lip had improved but was still present. One week later, the violaceous color of the papules and nodules was less intense. New papules and nodules appeared on the forehead, in the areas surrounding the ears, on the back and on the scalp. By this date almost the entire back was covered by discrete and confluent elongated large papules.

New lesions stopped appearing about two weeks after the quinacrine was discontinued. On May 13, a foul-smelling, weeping, pustular eruption began on the scalp. Within four days, it covered practically the entire scalp. Moist compresses of solution of boric acid, olive oil, hydrogen peroxide and penicillin had no beneficial effect. On May 18, Major F. T. Billings, surgeon in charge of the officers' ward, ordered 80,000 units of penicillin given intramuscularly. This dose was repeated in twenty-four hours. A dramatic response resulted, almost immediately the exudate and foul odor disappeared. Beta streptococci and hemolytic *Staphylococcus aureus* were cultured from the scalp exudate. By May 28,

the generalized infiltrated violaceous papules and nodules had become much flatter and more faded. All the finger nails were flat or spoon shaped, opaque, lusterless and deeply cross ridged. The mucous membranes of the mouth and lower lip were practically normal.

**CASE 5**—An American soldier, aged 26, began tropical service in October 1943. He had no physical disability or cutaneous disturbances until January 1944, when the tips of all his fingers became dry, thickened, hard and "cracked." Within a few weeks, the inner surfaces of both cheeks were tender and raw. When he was hospitalized, on Feb. 10, 1944, there were dry, scaly, exfoliating patches over all the surfaces of his fingers, hands and feet. The right commissure of the mouth was fissured and the lower lip superficially ulcerated. Except for the difficulty in eating and stiffness of his hands and feet, he had no other complaints.

On February 19, when he was transferred to a station hospital, macular, erythematous, pea-sized, dry, scaly lesions were present on the legs, and the hair of the scalp was matted by serum which oozed from moist, weeping plaques in the scalp. The foreskin of the penis was red, inflamed, tender and tight. The mouth was unchanged. One week later, the skin of the entire body became red and hot. His temperature rose to 100 F and he experienced several mild chills, although the weather was hot and he did not have malaria. The ankles soon became swollen, and he was too weak to walk.

On March 20, approximately three months after his eruption had started, he was admitted to this general hospital. It was readily apparent that he had lost considerable weight and was seriously ill. All the cutaneous surfaces were red, slightly edematous and scaly. In addition to the deep fissure of the right commissure of the mouth, superficial ulcerated, hypertrophic, grayish white plaques were present on both buccal mucosae and the dorsal and lateral surfaces of the tongue. Physical examination revealed moderate injection of the mucous membrane of the eyes, mouth and throat and moderate generalized lymphadenopathy. The lungs and heart were normal, and the liver and spleen were not palpable. A decubitus ulcer measuring approximately 2 cm in diameter was seen over the left hip.

Results of urinalyses and complete blood counts were normal. Serologic tests for syphilis elicited negative reactions. The van den Bergh test elicited a negative reaction, and ova and parasites were not found in the feces.

The patient had discontinued taking quinacrine hydrochloride on March 13. On March 23, infiltrated, slightly elevated and deeply violaceous plaques appeared in the suprapubic region and over both hips. Three days later, similar discrete and confluent plaques were generally distributed over practically all the body. The only free areas were the scalp and cheeks. This process involved the scrotum and the foreskin of the shaft of the penis, but the glans penis was clear. All the nails were yellow and heaped-up and presented transverse ridges. Subacute paronychia involvement occurred on every finger. Two days later, a moth-eaten type of alopecia was noticeable on the scalp, brows, axillae, pubic areas and other hair-bearing parts of the body. The generalized enlargement of lymph nodes progressed, the inguinal nodes being the ones most involved. Continually recurring exfoliation persisted. On April 20, the entire body surface was still hot and for the first time small scale-covered nodules appeared.

By May 10, the patient had passed through several stormy episodes. His temperature rose to 101.0 F, and



Fig 7 (case 6)—Mottled and solid pigmentation with rounded depigmented spots. The center of the back and the face were the only unaffected areas.

had appeared for two weeks. His temperature was normal, and he was no longer bedfast.

CASE 6—An Australian lieutenant, aged 35, began tropical service in the Southwest Pacific in August 1942. He had served in the Middle East from November 1940 to February 1942, during which time he had taken suppressive doses of quinine. When he entered the Southwest Pacific theater, he resumed the use of quinine and continued it until February 1943, when he began taking quinacrine hydrochloride. He was free of any cutaneous trouble until four months later (June), when itchy, pink, slightly elevated, discrete "welts" appeared on the belt line, legs and hands. The eruption was stationary for one month, but after the patient was treated for scabies with sulfur ointment, all his skin, except the face and a small patch on his back, became red and covered with a fine powdery scale. In one week, he had shed all his skin and most of the hair of the head, body and axillae. All the finger nails and toe nails became yellow and thickened. After the generalized desquamation, the skin began to weep and the patient experienced a generalized weakness. The shaft of the penis was involved by the weeping erythematous process, but the glans was normal. The ankles became swollen, and he complained of pain on defecation. After this process had continued to progress for two weeks, large, confluent, brown and violet infiltrated patches appeared. Generalized lymphadenopathy was present.

He was hospitalized July 29. On October 10, he was transferred to the One Hundred and Thirteenth Australian General Hospital. At this time, the violaceous color covered the entire body except the face, although the eyelids and ears were affected. A normal patch of skin remained in the interscapular space. He was unable to walk, and his temperature was 100 F.



Fig 8 (case 6)—Diffuse atrophy of the skin of the hands.

he was dehydrated. Constant nursing care was instituted, and after one week he appeared on the road to recovery. Meanwhile, increasing numbers of verrucous nodules appeared. In addition, pea-sized, grayish, warty excrescences were present chiefly over the thighs and lower part of the abdomen.

By about May 28, all signs of desquamation had stopped. No new verrucous nodules or warty excrescences

In November, he discontinued prophylactic malarial treatment. All the nails were shed, the hair of the scalp was sparse, and the rest of the body was devoid of hair. Deep blue warty excrescences appeared on the chest, back and legs. Generalized exfoliation occurred repeatedly. The pruritus, which had been so severe, was less of a problem. No lesions were present on the mucous membranes. In December, the elevated plaques

began to flatten and the warty excrescences became dry and brittle. The improvement was slow but progressive. Many of the warty pea-sized elevations fell off, and the elevated nodules and plaques flattened to the level of the surrounding skin. On April 26, 1944, all the infiltrated plaques had disappeared and only two warty excrescences remained. The scalp hair was normal and most of the axillary and pubic hair had returned. All the nails were normal. The most striking feature, however, was the generalized pigmentation which covered all the previously involved body surfaces. The pigmentation was both solid and mottled. It was made up of slate gray, blue and purple hues. A few rounded, depigmented spots, varying from 1 to 3 cm in diameter, were widely scattered over the chest, back and thighs. Small irregular patches of normal skin color were seen on the back, arms and thighs.



Fig 9 (case 6)—Close-up view of the back, showing reticulated atrophy

A diffuse atrophy was noticeable on both hands and feet. It was manifested by the presence of dry, wrinkled, reddish, thin skin. Although the skin appeared slightly transparent, telangiectasis was not present. In contrast to this diffuse atrophy of the extremities, a reticulated, or netlike, atrophy was seen on the torso.

The room was warm during the examination, and the previously uninvolved areas—that is, the face and the interscapular region—perspired profusely. At the same time the rest of the body, including the axillas, were powdery dry. The palms, which previously did not perspire, did so to a slight degree.

The general physical examination did not reveal anything abnormal. Results of laboratory procedures, including complete blood count, urinalyses, sugar tolerance test and determination of basal metabolic rate, were

all within normal limits. A blood film examined for malaria showed benign tertiary parasites, extremely scanty rings and ameboid forms. The serologic reaction for syphilis was negative.

The following case illustrates the rapid reversion of characteristic lesions on readministration of quinacrine hydrochloride.

**CASE 7**—An Australian soldier, aged 29, began tropical duty in January 1943. Six months later flat, dry, tan, scaly patches appeared on the extensor surfaces of the wrists and in the groins. Mycozol<sup>1</sup> and ointment of benzoic and salicylic acids were used without success. In rapid succession the arms, legs, chest, scalp, ears and neck became involved. Approximately six weeks after the appearance of the initial eruption, the patient experienced a soreness of his tongue on the ingestion of hot food or hot liquids. When he was hospitalized, four weeks later, the face, except for the eyelids, was the only unaffected portion of the entire body. Repeated desquamation of all cutaneous surfaces was occurring. A brown to purplish red color was now present in many scaly patches which had become infiltrated. Later, deeply pigmented, pea-sized, sessile, warty excrescences appeared on the abdomen and thighs. The finger nails were loosely attached, and several had fallen out. A patchy alopecia was present on all hair-bearing surfaces.

On October 7, when he was admitted to the One Hundred and Thirteenth Australian General Hospital, his entire body except for the face presented a red to violaceous hue with many widespread, elevated, deeply violaceous papules, nodules and plaques. The dorsum of the tongue contained two elongated, elevated, white streaks. The larger measured 2.5 by 1 cm. No lesions were present on the glans penis. The entire body and scalp were devoid of hair. All the finger nails and several toe nails were missing.

Except for the observation of profuse sweating of the face and the absence of sweating elsewhere, physical examination revealed no additional significant conditions.

Except for the finding of malarial parasites, all laboratory values were within normal limits.

Use of quinacrine was discontinued, and in two weeks new elevated lesions ceased to appear. In approximately one month, the lesions of the tongue had vanished, and many of the elevated purplish patches had become duller and flatter. About four months was required for all the elevated lesions to flatten and become transformed into grayish blue macular or atrophic stained patches. Many of the warty excrescences fell off en masse, but others persisted unchanged.

On Feb 2, 1944, he experienced malarial chills, and quinine was administered for three days without any untoward reaction. On the fourth day, quinine was discontinued, and 0.1 Gm of quinacrine hydrochloride was given three times daily. On the morning of the third day of administration of quinacrine, many old papules and nodules on the arms became red, warm and slightly elevated. Generalized severe itching also occurred. Quinacrine was continued for five days. Five days later, it was again given, 0.1 Gm daily, and its use was continued for thirty-six days. The aggravation of the eruption continued for two weeks, then

<sup>1</sup> A proprietary preparation of the following composition: chlorobutanol, 5 per cent, salicylic acid, 4 per cent, mercuric salicylate, 4 per cent, and aromatic substances and ointment base, to make 100 per cent.

his condition remained stationary. The tongue again became tender.

In May 1944, when he was last seen, a generalized, mottled, grayish blue and tan staining was present. Some clear areas were noted. Macular negroid patches varying in size from 0.2 to 2 cm were seen on the posterior surfaces of the neck and shoulders. A complete regrowth of hair was present on the scalp. Incomplete regrowth of hair was observed on the torso. Diminished sweating took place in the axillas and palms. There was no change in the atrophy.

#### COMMENT

The interval between starting the drug and the appearance of the eruption was in no case less than one month, the longest interval was eleven months, and the average interval was three and one-half months. There was no relationship between this interval and the severity of the eruption, for some of the patients with severe eruptions had taken the drug only two months.

The length of the period during which use of the drug was continued after the eruption appeared was probably more important in relationship to the severity of the eruption. Continued study of a larger series of cases will be necessary to determine this association definitely. We observed that the milder eruptions usually occurred in the patients who discontinued taking the drug immediately after the appearance of characteristic lesions.

That the dosage influenced the occurrence of the eruption was demonstrated by some persons who tolerated the routine prophylactic dosage for long periods. But when the prophylactic dose was increased or when they took larger quantities of the drug to combat malarial symptoms, the eruption appeared within two weeks. This might indicate a saturation level and toxicity of the drug rather than idiosyncrasy or intolerance to it. Also favoring this hypothesis was a failure of a single dose of the drug to cause a recurrence of the eruption in patients who had previously had clearing. Use of the drug had to be continued at least two days before the cutaneous eruption reappeared. This might also suggest that a cumulative action takes place.

We do not feel that the failure of the typical papules to appear two weeks after readministration of quinacrine hydrochloride in 3 cases rules out the drug as the causative agent. Refractory periods have been described in many drug eruptions. Also it is likely that the toxic blood level had not been reached during the two week period of readministration.

Undoubtedly other variants of this syndrome than those presented in this study have occurred but have not yet been recorded.

The prognosis in all cases is good so far as life is concerned, for no fatalities occurred. The prognosis of acute exfoliative dermatitis is always guarded, toxic symptoms may develop and result in a fatal termination. Unexplained recurrences of the exfoliative process may occur. The widespread disfiguring pigmentation of the severe eruptions is of serious importance. One patient had the onset of his eruption eleven months ago and another patient nine months ago. The grayish blue and rust-colored generalized pigmentation has become lighter, and patches approaching the color of normal skin are present. But both men are still badly disfigured and could be suitable material for a "freak show." The milder eruptions cleared with depigmentation or light gray to deep blue hyperpigmentation with or without cutaneous atrophy. The atrophy is a nonreversible process and represents a permanent disability in persons with severe eruptions. Partial return of function of the sweat glands is a hopeful sign. Regrowth of the hair of the scalp, axillas and groins occurred in every case. Up to the time of this writing, regrowth of the hair of the torso and extremities had not occurred in 3 men with severe involvement who were observed over a period of seven to eight months. Normal replacement of nails took place in every instance.

Photosensitization did not enter the problem, because the exposed parts were not affected out of proportion to the covered surfaces.

There did not appear to be any relationship between the described eruption and the ordinary universal lemon to saffron yellow staining of the skin which occurs in almost every person who takes quinacrine hydrochloride for a prolonged period.

It will be known whether tropical conditions are essential in the production of this disease when the experiences of medical officers in non-tropical theaters where quinacrine is regularly used are learned.

The many forms which the early eruption assumed is not in itself a new phenomenon, for it has long been known that a single drug can produce many different eruptions in the same subject or in different subjects.

#### SUMMARY AND CONCLUSIONS

1 A previously unreported cutaneous syndrome produced by quinacrine hydrochloride has been observed.

2 The incidence is extremely low. Nothing in this study would indicate that the present suppressive and treatment routine with quinacrine should be altered.

3 This eruption frequently closely resembles atypical forms of lichen planus. We believe that sufficient variations have been pointed out to differentiate clearly and definitely these diseases.

4 It is extremely important that this syndrome be known and readily recognized by military physicians because

- (a) Early discontinuance of the drug may prevent serious involvement and prolonged disability
- (b) Improvement or clearing of the eruption will not result unless use of the offending drug is stopped
- (c) When the question of disposition of an affected person arises, the medical examiner will know that tropical service requiring the resumption of use of quinacrine is dangerous, and if it is avoided the person will be suitable for nontropical duty

5 Scientific experimental research should be carried on now because the clinical material and circumstances will not always be available.

Colonel W. Wood, Medical Corps, Australian Army, former Commanding Officer of the One Hundred and Thirteenth Australian General Hospital, Colonel Morris Jacobs, Medical Corps, Australian Army, Commanding Officer of the One Hundred and Fourteenth

Australian General Hospital, Colonel Douglas Thomas, Medical Corps, Australian Army, Commanding Officer of the One Hundred and Fifteenth Australian General Hospital, Colonel Thomas McP. Brown, Medical Corps, Army of the United States, former Commanding Officer of the One Hundred and Eighteenth American General Hospital, and Lieutenant Colonel J. Boardly, Medical Corps, Army of the United States, present Commanding Officer of the One Hundred and Eighteenth American General Hospital, and Captain Alva Smith (MC), USNR, Commanding Officer of the United States Naval Base Hospital No. 10, allowed us to observe and study patients in their hospitals.

Major L. Katzenstein, Medical Corps, Army of the United States, dermatologist of the One Hundred and Eighteenth American General Hospital, cooperated in the study of the patients in his wards. Major L. Utz, Medical Corps, Australian Army, of the One Hundred and Thirteenth Australian General Hospital, and Lieutenant Colonel W. B. Vandergrift, Medical Corps, Army of the United States, of the One Hundred and Eighteenth American General Hospital, assisted by furnishing the laboratory information and preparing the sections for microscopic study. Lieutenant Colonel A. L. Dawson, DSO, visiting dermatologist of the One Hundred and Thirteenth Australian General Hospital, and Major John Ambler, Medical Corps, Army of the United States, dermatologic consultant for the American forces in the Southwest Pacific, made valuable suggestions.

The photographic illustrations were made by Mr. Woodward Smith, of the Department of Medical Artistry, University of Sydney, School of Medicine.



# BETA DIMETHYLAMINOETHYL BENZHYDRYL ETHER HYDROCHLORIDE (BENADRYL) IN TREATMENT OF URTICARIA

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Considerable evidence has been presented by Lewis<sup>1</sup> to support the conclusion that a diffusible substance is responsible for the development of the urticarial lesion which comprises "the triple response" of local vasodilatation, flare and eventually local edema. This material, which is called the H substance, is liberated by injured cells and closely resembles histamine in its action. It apparently causes the local vasodilatation and wheal by direct action on the capillary wall and the flare by the chemical stimulation of the sensory ending of the skin, bringing about widespread arteriolar and venous dilatation through the mechanism of the axon reflex. Support of this theory has been offered by others<sup>2</sup>. However, the evidence that histamine is the urticariogenic substance is indirect. It has never been isolated from a wheal, and not all investigators agree that it plays any part in the development of the wheal<sup>3</sup>.

Recently there has been synthesized a substance which belongs to a new and distinct pharmacologic group of compounds. These substances are antispasmodics, and one at least has a profound antihistamine effect.

The substance used in our studies is beta dimethylaminoethyl benzhydryl ether hydrochloride, which has been given the name of Benadryl<sup>4</sup>. It is white, crystalline, water-soluble powder which is stable under ordinary conditions. When it is given intraperitoneally, it is fifteen to thirty times more active than theophylline ethylenediamine in lowering the mortality of guinea pigs

subjected to lethal doses of histamine and it is also much more active in reducing bronchospasm. In reducing smooth muscle spasm, it is six hundred and fifty times more effective than papaverine hydrochloride, fifty times more effective than acetylcholine bromide and one and three-tenths times more active than barium chloride<sup>5</sup>.

Benadryl appears to have a low toxicity. Death occurs in 50 per cent of albino mice after an oral dose of 167 mg per kilogram and in albino rats after 545 mg per kilogram. Lethal doses were followed by violent excitement, convulsions, respiratory failure and death in a few minutes to several hours. Excitement and ataxia occurred after nonlethal toxic doses, and recovery occurred in one to two hours. It is also possible to administer the drug parenterally in smaller doses without local tissue damage. From 10 to 60 mg per kilogram was given orally to dogs for thirty-seven to forty-nine days. There was no change in eating habits, weight, blood counts, hemoglobin and nonprotein nitrogen values. After prolonged ingestion of the drug, the dogs showed at autopsy no abnormal conditions due to its intake<sup>4</sup>.

The pharmacologic studies showing the antihistamine effect of Benadryl produced such striking results that we thought the drug might have distinct value in controlling urticaria. If this assumption proved true, it also might add to the indirect evidence that histamine is a factor in the production of urticaria. The following cases are a few of those in which Benadryl was used.

CASE 1—J. A., a 43 year old man, was first seen on Aug. 3, 1944, with the diagnosis of probable peripheral vascular disease. He had had chronic urticaria of the arms, back and legs for two and one-half years, for which there had been no previous specific treatment. Benadryl, 50 mg three times a day, afforded no relief, but use of 100 mg three times a day was followed by definite improvement within thirty-six hours. Only an occasional lesion appeared when this dose was continued for four days. When the drug was stopped,

5 Loew, E. R., Kaiser, M. E., and Moore, V. Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine, *J. Pharmacol. & Exper. Therap.* 83:120, 1945.

Studies and contributions from the Department of Dermatology and Syphilology of the University of Michigan, service of Dr. Udo J. Wile.

1 Lewis, T. *The Blood Vessels of the Human Skin and Their Responses*, London, Shaw & Sons, Ltd., 1937.

2 Dale, H. H., and Laidlaw, P. P. Histamine Shock, *J. Physiol.* 52:355, 1919; The Physiological Action of B. Imminazolyethylamine, *ibid.* 41:318, 1910; Further Observations on the Action of B. Imminazolyethylamine *ibid.* 43:182, 1911.

3 Alexander, H. S., Harter, J. O., and McConnell, F. S. Observations on the Formation of Wheals, *Proc. Soc. Exper. Biol. & Med.* 29:484, 1930.

4 Dept. of Clin. Investigation, Parke, Davis & Company. Personal communication to the authors.



the urticaria promptly recurred. No reactions to the drug appeared.

CASE 2—I E, a 41 year old white woman, was admitted to the University Hospital on June 30, 1944, with a tentative diagnosis of periarteritis nodosa. There had been chronic urticaria for two years. Ephedrine and amytal, succinylsulfathiazole and cathartics had not improved the eruption. Benadryl, 50 mg three times a day, gave relief in two hours. Use of the drug was later discontinued, and a recurrence of lesions followed. Resumption of the drug caused the urticarial eruption to disappear promptly. The drug was taken for seven months, and no lesions occurred. Drowsiness and muscular aching were noted while the drug was administered, but no other reactions occurred.

CASE 3—S B, a 64 year old woman (private patient), was seen Jan 2, 1945, with a twelve week history of generalized giant urticaria and recurrent angioneurotic edema of the hands, eyes and larynx. Her only treatment had been with magnesium sulfate, without effect. She gave a vague history of qualitative dyspepsia and pain in the right upper quadrant of the abdomen. Roentgenologic examination confirmed a diagnosis of cholelithiasis. After administration of 50 mg of Benadryl three times daily, the urticarial lesions disappeared promptly, and only a rare one occurred in two months of continuous administration of the drug. No toxic reactions to the drug were noted.

CASE 4—C R T, a 49 year old woman (private patient), was seen on Jan 26, 1945, with a five months' history of widespread urticaria which appeared almost every night. The lesions usually persisted for four or five hours, but at times they lasted two or three days. She had avoided feathers and had had patch tests with many substances which had not revealed the etiologic agent. Fifty milligrams of Benadryl three times a day resulted in rapid clearing, with only a rare lesion appearing during the following nine days. When use of the drug was discontinued, the urticarial lesions recurred. No untoward reactions from the drug occurred.

CASE 5—W W, a 40 year old woman (private patient), gave a six months' history of giant urticaria and angioneurotic edema on Nov 1, 1944. Many drugs and elimination diets were tried without effect. For one month the urticaria disappeared and did not recur when she took 50 mg of Benadryl four times a day, but a few wheals would reappear if she took only 50 mg three times a day. Use of the drug was then discontinued for three weeks, with recurrence of the lesions. Resumption of Benadryl was followed by complete relief, but she required 50 mg five times daily. No reaction to the drug occurred.

CASE 6—C D, a 31 year old woman, was seen on Aug 10, 1944, with a history of chronic urticaria, and dermatographia for seven years. Drugs and elimination diets had no effect. Use of Benadryl, 50 mg three times a day, was followed by a prompt subsidence of her symptoms in two days. After one month of 150 mg daily, the dose was lowered to 50 mg, with which the symptoms were controlled for five months. Urticarial lesions recurred if a capsule was not taken daily. No unfavorable reaction to the drug occurred.

CASE 7—P S, a 16 year old girl, was seen Nov 18, 1944, with generalized urticaria and occasional angioneurotic edema of fifteen years' duration. Although the lesions would occur spontaneously, exposure

to cold would definitely precipitate an attack. Elimination diets and drug therapy had no effect. Benadryl, 50 mg four times a day, was given for one week, during which time only a single urticarial wheal appeared. During the next five days she had a few lesions. The drug was then discontinued, with prompt recurrence of her symptoms. After resuming the use of Benadryl, she again had clearing except for an occasional urticarial lesion. No sensitivity to the drug resulted.

CASE 8—A G, a 50 year old white man, was seen Feb 8, 1945, with a history of daily itching of the body and severe dermatographia for ten years. There had been no previous treatment. Examination revealed numerous welts on the body where he had been scratching. Two hours after an oral dose of 50 mg of Benadryl, the itching subsided, and with the dosage of 50 mg three times a day for one week, there was no occurrence of pruritus or noticeable dermatographia. He then voluntarily discontinued taking the drug, with no recurrence of pruritus, and he did not notice dermatographia. However, three days after ingestion of the drug was stopped, typical wheals could be demonstrated after the skin was stroked lightly but pruritus did not appear. There were no toxic symptoms from the drug.

CASE 9—M F, a 22 year old man (private patient), presented himself on Feb 20, 1945, with a two months' history of urticaria. One or two lesions appeared at any site on the body and lasted for two or three days. He was never free of lesions. The initial dose of Benadryl, 50 mg, was followed by disappearance of the urticaria in one hour. Fifty milligrams three times a day was administered for seven days, during which time no lesions appeared. Administration of the drug was discontinued, and in two days several pruritic urticaria appeared. Benadryl, 50 mg twice a day and then 50 mg daily, was administered, with no urticarial lesions appearing in eight days. Drowsiness and muscular soreness were present while the drug was ingested, but the patient was able to take the one dose at night and the toxic symptoms subsided by the time he arose in the morning.

CASE 10—J J, a 68 year old man with carcinoma of the tongue, was seen on Jan 26, 1945. He complained of generalized urticaria of four years' duration. The urticarial lesions were never absent for longer than three days. Benadryl, 50 mg, was followed by disappearance of lesions in three hours. The drug was continued in the dosage of 50 mg three times a day for thirty-one days with no recurrence. Six hours after discontinuation of Benadryl, generalized urticaria with pruritus reappeared, it continued for three days at which time the drug was again administered, with complete relief. No toxic reactions to the drug occurred.

CASE 11—F B, a 75 year old man with prostatism and cystitis, was seen on Feb 5, 1945, with an acute generalized giant urticaria of two days' duration. He had taken 0.6 Gm of pentobarbital sodium on the first day of the urticarial eruption. Two hours after he had taken 50 mg of Benadryl, the itching subsided, but generalized urticaria remained for three or four hours and then disappeared. After three days of use of Benadryl, 50 mg three times a day, the drug was stopped, with no recurrence of lesions. There was no intolerance to the drug.

CASE 12—R P, a 34 year old man, was seen Sept 4, 1944, with recurrent giant urticaria of six months' duration. He had been treated unsuccessfully with

epinephrine hydrochloride, foreign injections of protein and calcium. Infected teeth were removed without relief. Benadryl, 50 mg three times a day, gave dramatic relief, which occurred one to two hours after the taking of the initial dose of 50 mg. Each time use of the drug was discontinued giant urticaria unrelieved by epinephrine reappeared. While taking Benadryl he continued to have occasional urticarial lesions, most of which were not pruritic. He varied the dosage from 50 to 100 mg three times a day, depending on the symptoms, but he still had to take it to remain asymptomatic. No idiosyncrasy to the drug occurred.

CASE 13—R K, a 49 year old woman, was seen June 20, 1944, with chronic generalized giant urticaria of five months' duration. Succinylsulfathiazole had been administered previously and caused no improvement. Benadryl, 50 mg three times a day, gave dramatic relief for two weeks. She then stopped taking the drug, and urticaria recurred. In four days use of Benadryl was again instituted and significant improvement resulted, but the symptoms were not entirely controlled by even 100 mg three times a day. However, many of the urticarial lesions were not pruritic. After discontinuance of the administration of the capsules for three days, a giant urticarial lesion developed on the upper lip. The swelling and pruritus were seen to disappear within one-half hour after 100 mg of Benadryl was given. No toxic symptoms occurred while the drug was given.

CASE 14—I I W, a 22 year old woman, was admitted to the University Hospital on Feb 22, 1945. Three years previously she began having generalized urticaria for the two weeks before the menstrual periods. For the four and one-half months before admission she had generalized urticaria continuously. Use of Benadryl, 100 mg, was followed by cessation of itching in fifteen minutes and disappearance of wheals in forty-five minutes. Benadryl, 100 mg, three times a day, was given for five days. All pruritus disappeared, but red wheals appeared on the skin about four hours after a dose of Benadryl and disappeared immediately after the next dose. A placebo was given on one occasion in place of the drug, and typical pruritic urticarial wheals occurred two hours afterward, seven hours after the last administration of Benadryl. These were relieved immediately by 100 mg of Benadryl. No toxic reactions to the drug occurred.

CASE 15—A C, a 45 year old man, gave a history of the development in 1936 of chronic urticarial lesions, which lasted about eight months. Five months before his admission to the University Hospital, on Sept 2, 1944, he again had urticaria, which remained recurrent. No foci of infection were found. Ephedrine and amital, magnesium sulfate and succinylsulfathiazole were used without effect. Benadryl, 50 mg three times a day for one week and then 100 mg for one week, was given without effect. No sensitivity to the drug occurred.

CASE 16—R D, a 14 year old boy, was seen Sept 8, 1944, with chronic urticaria which he had had for one year. Various internal medicines, injections and diets had not improved his condition. An infected tooth was removed, but no improvement occurred. Benadryl, 50 mg twice a day for six days and then four times a day for nine days, gave no relief. No toxic reactions to the drug were noted.

CASE 17—V E, a 62 year old diabetic woman, was seen Aug 11, 1944, with giant urticaria and recurrent laryngeal edema present for six months. Injections of

liver, calcium and nicotinic acid had not been effective. Dietary elimination was also valueless. Benadryl, 50 mg three times a day, was given for one week, with disappearance of itching but persistence of red "blotches" and small hives. She then took a large dose of acetylsalicylic acid, which was followed by severe laryngeal edema and generalized giant urticaria. Following this, giant urticaria persisted in spite of 100 mg of Benadryl three times a day for two weeks. There were no toxic symptoms from the drug.

CASE 18—W R, a 26 year old man, was seen Oct 28, 1944, with generalized urticaria of fifteen years' duration. The urticarial lesions invariably occurred when he changed from a cool to a warm environment. Benadryl, 50 mg four times a day for one week, effected no change. Dizziness, weakness and vertigo occurred, and use of the drug was therefore stopped.

#### COMMENT

Eighteen patients with various types of urticarial eruptions were treated with Benadryl. While taking the drug, 11 responded with complete disappearance of the urticaria, except for an occasional nonpruritic lesion which would appear for a short time. Three patients had enough real improvement to warrant continuation of the drug, and in these patients a large number of the wheals were not pruritic. Four patients did not respond to the doses given. In only 1 case were there toxic symptoms of weakness and vertigo severe enough to necessitate the discontinuance of the drug. The symptoms disappeared promptly when use of the drug was discontinued. Two patients complained of drowsiness and muscular aching, but 1 continued to take benadryl for seven months without other ill effects. Two other patients took the drug for six months and two months respectively without any toxic symptoms.

Benadryl is palliative only. Chronic urticaria, pruritus, angioneurotic edema and dermatographia recur promptly when use of the drug is discontinued. Since the determination of the cause and subsequent cure of chronic urticaria is often impossible or at best a long, painstaking procedure under the present methods, this drug offers symptomatic relief to many patients. It was effective in aborting acute urticaria. The specific effect of the drug was the disappearance of the eruption when it was administered and the prompt recurrence of the eruption in chronic urticaria when it was discontinued.

Preliminary studies would seem to indicate that benadryl should be tried for other types of allergic disease. The drug appears to be of value for erythema multiforme.

#### SUMMARY AND CONCLUSIONS

1 Beta dimethylaminoethyl benzhydryl ether hydrochloride (Benadryl) is a member of a new

group of pharmacologically active antihistamine drugs

2 Its use in amounts of 50 to 100 mg given orally one to five times daily to a diverse group of 18 patients with both acute and chronic urticaria is reported

3 Eleven patients experienced prompt relief of symptoms as long as the drug was taken. Three had definite and real improvement, and many of the wheals which did appear were not pruritic. Four patients were not benefited.

4 The drug has a wide margin of safety, and the only toxic manifestations noted were drowsiness and muscular aching (2 cases) and dizziness,

weakness and vertigo (1 case). No cumulative toxic symptoms were noted in patients who ingested the drug as long as six or seven months. All toxic symptoms promptly disappeared when the drug was discontinued.

5 The effect is palliative, and in many patients the urticaria recurred when the administration of the drug was discontinued.

6 Since an antihistamine drug seems to be effective in controlling urticaria it may be assumed that this is further indirect evidence that histamine is a factor in the production of urticaria.

# USE OF BENADRYL FOR URTICARIA AND RELATED DERMATOSES

## A PRELIMINARY REPORT

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DETROIT

Symptomatic relief of urticaria and allied manifestations of cutaneous allergy is essential to the management of such dermatoses while a search for their cause is being made. The use of epinephrine, ephedrine and sedatives is often contraindicated or unsatisfactory. Attempts at desensitization to histamine have proved disappointing. We are therefore making this preliminary report to call attention to a new drug which shows promise, we believe, in the management of such eruptions.

### PHARMACOLOGY

Benadryl<sup>1</sup> (beta dimethylaminoethyl benzhydryl ether hydrochloride) antagonizes the effects of histamine on smooth muscle of the bronchioles and intestines of guinea pigs and effectively alleviates histamine shock in these animals.<sup>2</sup> It is a white crystalline powder, soluble in water and alcohol, and is stable under ordinary conditions of temperature and atmosphere. The preparation is well tolerated by animals in many times the dosage recommended for man. The maximum response occurs in about twenty to sixty minutes after oral administration and lasts for from five to eight hours. It is recommended that for human beings 50 mg (1 capsule) be administered orally three or four times daily. On the basis of experimental work it was suggested that Benadryl should prove valuable in the control of asthma, hay fever, urticaria and spastic conditions in human beings.

### CLINICAL OBSERVATIONS

Release of histamine in the cutis is recognized as the trigger mechanism in the production of

urticaria. It may also be a factor in related allergic cutaneous responses such as lichen urticatus, atopic eczema and erythema multiforme. It was decided, therefore, to test the therapeutic effect of Benadryl in the management of such eruptions, especially urticaria.

#### *Urticaria*

CASE 1—K H, a Negro man aged 31, first had urticaria during the summer of 1929. There was a spontaneous remission for a time, but the disease recurred during the summer and fall of 1930. During that period he had one severe attack lasting three days which involved the glottis and almost caused suffocation. He had another attack of urticaria in June 1937, which lasted one week. No cause for these attacks was discovered. He was admitted to Receiving Hospital in August 1944, and urticaria developed following a thyroidectomy. Again, no etiologic factors were demonstrated. He was released from the hospital while still suffering from urticaria and reported to the outpatient department one week later. He was given an oral dose of 1 capsule (50 mg) of Benadryl four times a day plus calamine lotion containing 1 per cent phenol. He returned to the clinic three weeks later because his supply of Benadryl was exhausted and his urticaria had recurred. At that time he stated that the pruritus subsided one-half hour after the first capsule was taken and the wheals disappeared eight hours later. He has followed the same dosage schedule for eleven weeks since that time without untoward effects, and the urticaria has been kept under control. During a two week period he was given placebo capsules instead of the Benadryl. During this time he had a severe recurrence of the urticaria, which promptly subsided when he was returned to the Benadryl schedule.

CASE 2—L C, a white boy aged 13 months, had an acute generalized urticaria. Calamine lotion was applied locally, without relief from pruritus, and the child cried and scratched continuously. He was then given orally the contents of ½ capsule of Benadryl (approximately 25 mg) dissolved in a teaspoon of water. One-half hour later the pruritus apparently subsided, and the child fell asleep. The next morning the skin was clear, and there has been no recurrence.

CASE 3—T W, a white woman aged 52, had a recurrent urticaria for four months. During an acute flare-up she was given an oral dose of one 50 mg capsule of Benadryl four times a day. No other treatment was given, systemic or local. The pruritus subsided within two hours after the first dose of Benadryl was taken, and the urticarial lesions had completely disappeared forty-eight hours later. The patient has been taking the drug intermittently for the past three months.

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1 Developed and supplied for clinical trial by Parke, Davis & Company, Detroit.

2 Loew, E R, Kaiser, M E, and Moore, V. Synthetic Benzhadryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Subjected to Vaporized Histamine, *J Pharmacol & Exper Therap*, to be published.

to control the urticaria. She has hypertension (blood pressure of 204 systolic and 130 diastolic) which had previously interdicted the use of epinephrine or ephedrine.

CASE 4—A B, a white man aged 32, had urticaria of undetermined cause for four months. He was given no local therapy and was advised to take an oral 50 mg dose of Benadryl four times a day, but he voluntarily reduced it to twice a day because of the sedative effect which he experienced. On this reduced dosage schedule, however, the pruritus and wheals subsided twenty-four hours after the first capsule was taken. The lesions promptly returned as soon as he stopped taking the Benadryl and disappeared just as promptly when use of the drug was resumed.

CASE 5—H R, a Negro woman aged 30 had urticarial lesions of one week's duration scattered over the body. The cause was undetermined. She was given calamine lotion for local use and a magnesium sulfate cathartic. She was also given an oral dose, 50 mg, of Benadryl four times a day. Five days later the urticaria had completely cleared and the patient stated that she had experienced no untoward effects from the drug. She has not been seen since.

CASE 6—C H, a white woman aged 38, had a generalized urticaria of two days' duration. She was given 1 Benadryl capsule, 50 mg, orally four times daily plus calamine lotion locally. Ten hours after she had taken the first capsule the pruritus began to subside and relief was complete in twenty-four hours. In six days there was complete involution of the urticarial lesions. Use of Benadryl was then discontinued, and the urticaria has not recurred. In this case the sedative action of the drug was noticeable.

CASE 7—M D, a Negro woman aged 20, had pyelitis, nephrosis and a generalized folliculitis secondary to the renal focus of infection. The pyelitis and folliculitis responded to a course of 575,000 units of penicillin, and she was then given injections of staphylococcus toxoid and autogenous vaccine. While she was receiving the latter therapy, a generalized urticaria developed. Use of the vaccines was discontinued, and the patient was given an oral dose of 50 mg of Benadryl every four hours daily for a total of seventeen doses. The pruritus and wheals subsided within twelve hours after the first dose and did not recur. After the drug was stopped, the urticaria did not recur.

CASE 8—A H, a white man aged 52, has had angina pectoris for the past ten years. He also has psoriasis and for the past month has had recurrent urticaria. He has been taking nitroglycerin frequently for the past two months. The angina pectoris interdicted the use of epinephrine or ephedrine, so he was given Benadryl for two weeks while in the City of Detroit Receiving Hospital. During the first week, while he was taking a 50 mg capsule of Benadryl four times a day, there was a noticeable decrease in pruritus and number of wheals, but thereafter he continued to have a recurrence of the urticaria, even though the drug was increased to 1 capsule every four hours around the clock for three days and then 1 capsule every two hours for seven doses daily for the next four days.

### *Lichen Urticatus*

CASE 1—H H, a Negro woman aged 24, has had a chronic generalized eruption for many years consisting of persistent urticarial lesions, bullae, pruritus and some atrophy. She is sensitive to many foods, especially milk, pork and oranges. Iris lesions have occurred at one

time or another over the entire body, leaving the skin atrophic and wrinkled in many places, especially on the dorsa of the hands and forearms. There has been much discussion as to the diagnosis in this case. Classification of the eruption as chronic lichen urticatus with urticaria and erythema multiforme characteristics is most acceptable. Besides various forms of local therapy and removal of possible foci of infection, attempts have been made at histamine desensitization with histamine azo protein by injection. The latter has been only partially successful, and, owing to her failure to attend the clinic regularly, the patient has had frequent relapses. During a recent flare-up she was given 50 mg of Benadryl by mouth three times a day. When she was seen again two days later, after she had taken 6 capsules, the pruritus had disappeared and an iris-like lesion on the face had completely disappeared.

### *Eczema*

CASE 1—B K, a white woman aged 51, had eczema for five years involving the flexor surfaces of the forearms, the cubital fossae, the popliteal areas and the mammary folds. The cause was not discovered, although the eruption was considered as belonging in the neurodermatitis group. She failed to respond to the usual methods of local treatment and was given a 50 mg capsule of Benadryl four times daily. The pruritus subsided after two and one-half days' use of the drug. The eczema cleared completely in twenty days, and the skin remained clear as long as she continued to take Benadryl. She was seen recently, and a recurrence had developed after she had not taken the drug for one week. The previous dosage schedule was resumed, but the pruritus and eczema have persisted.

CASE 2—L K, a white physician aged 34, has had a generalized atopic eczema for thirty years and has failed to improve with all types of therapy throughout these years. He required sedation for sleep, and his skin would tolerate only the mildest soothing applications. Soap and water could not be used, and there was a constant fine scaling of the skin. He was given an oral dose of 50 mg of Benadryl four times a day and in two weeks many areas of normal-appearing skin were visible and no new areas of eczema or fissuring developed. The pruritus had lessened greatly and the patient was able to sleep without the aid of hypnotics. His skin felt softer than previously, even though the weather was cold and the eczema was always worse during the winter months. After taking Benadryl for five weeks he was able to take his first shower bath in two years. At the time of this writing the eczema is steadily improving, objectively and symptomatically. As to untoward effects in this case, there were none save a thickening of the bronchial secretions and decrease in salivation. The latter was overcome by chewing gum.

CASE 3—H K, a white physician, aged 27, has recurring dyshidrotic eczema of the hands and fingers of seventeen years' duration. Local therapy and low voltage roentgen irradiation have resulted in only temporary improvement. He was given a 50 mg capsule of Benadryl four times a day for ten days, without improvement. On the tenth day a new group of vesicles appeared on the fingers, and the patient, feeling that the drug was of no value in his case, discontinued treatment.

CASE 4—M T, a white woman aged 26, presents a chronic neurodermatitis with lichenified plaques on the back of the neck and the flexor surfaces of the

elbows and knees and excoriations on the thighs and the upper part of the trunk. The face was erythematous and was covered with scratch marks. Her eruption has been present for nine years, and she has a definite psychoneurotic background. Besides bland local therapy, she was given a 50 mg capsule of Benadryl four times a day for one week, with no effect on the pruritus or the dermatitis.

#### COMMENT AND CONCLUSIONS

From the cases described it would seem that the antihistamine action of Benadryl exerted a beneficial effect in the control of the pruritus and the involution of the lesions of urticaria within a fairly short period. Compared to the neurovascular stimulating action of epinephrine and ephedrine, Benadryl apparently produced no untoward effects, especially on the blood pressure, and, in some instances, had a sedative

action. The favorable therapeutic effect in 7 of the 8 cases of urticaria presented suggests that this drug may prove effective in the palliative relief of urticaria. In acute cases such palliation may be all that is required for their management. In cases of chronic urticaria it might offer valuable relief until investigation reveals the cause and adequate control measures can be carried out.

Two cases of neurodermatitis, 1 of dyshidrotic eczema, 1 of atopic eczema and 1 of chronic lichen urticatus are hardly sufficient to appraise the value of Benadryl for these diseases. However, our limited experience would suggest that it is of no value for neurodermatitis or dyshidrotic eczema. Results obtained by its use for atopic eczema and lichen urticatus warrant further trial.

# PENICILLIN OINTMENT

## STUDIES ON STABILITY RELATIVE TO POTENCY AND ON THE SENSITIVITY OF THE HUMAN SKIN TO PATCH TESTS WITH OINTMENT

LIEUTENANT COMMANDER RALPH B COOMBER (MC), USNR

The literature has shown an increasing utilization of penicillin in several forms in the treatment of diseases of the skin. With its use, many types of cutaneous disease have shown a surprising response. Fleming<sup>1</sup> reported that in the laboratory he found penicillin about ten times as effective as sulfathiazole as an antibacterial agent. Clark, Colebrook, Gibson and Thompson<sup>2</sup> applied penicillin in the form of a cream to fifty-four burns and scalds in various stages of healing with a view to the elimination of hemolytic streptococci, and in 76 per cent of the wounds these organisms disappeared within five days and did not reappear. There were no cases in which the application of penicillin appeared to have no effect. Healings were unusually rapid, and no toxic effects were observed.

Experiments have demonstrated that penicillin in a liquid form loses its potency on standing. Abraham<sup>3</sup> found that the barium salt of penicillin in aqueous solution with a  $p_H$  of 5.5 to 7.5 retains its activity for several months at 2 C, for several weeks at 25 C, for twenty-four hours at 37 C and for thirty minutes at 100 C. Dissolved in either amyl acetate or ether it is stable for several days at room temperature.

Inasmuch as penicillin is now being used and later will be used extensively in ointment form, the question arises as to its degree of stability in this form compared with the degree of stability in liquid form. While studying this problem, I decided to determine the degree of tolerance exhibited by the skin to penicillin in ointment form.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The views set forth are those of the authors and are not to be construed as reflecting the policies of the Navy department.

1 Fleming, A, in discussion on Chemotherapy for War Wounds, Brit M J 2 640 (Nov 9) 1940

2 Clark, A M, and others. Penicillin and Propamidine in Burns. Elimination of Haemolytic Streptococci and Staphylococci, Lancet 1 605 (May 15) 1943

3 Abraham, E P, and Chain, E. Purification and Some Physical and Chemical Properties of Penicillin, Brit J Exper Path 23 103 (June) 1942

### EXPERIMENTAL METHOD AND RESULTS

Powdered calcium penicillin was dissolved in sterile distilled water to a concentration of 10,000 units per cubic centimeter. This solution was then added to hydrous wool fat to a point that 1 cubic centimeter of the solution was absorbed by 1.3 Gm of hydrous wool fat. This gave a concentration of approximately 4,350 units per cubic centimeter.

Into a sterile Petri dish was poured a medium composed of melted nutrient agar to which was added 1 cubic centimeter of a broth culture of hay bacillus. As the medium solidified, glass cylinders 1 cm in length and 4 mm in diameter were inserted. Each day one cylinder was filled with an ointment which had been kept at room temperature, another was filled with an ointment which had been refrigerated at approximately 15 C and a third was used as a control. The plates were then incubated for twenty-four hours, after which the width of the zone of inhibition or clearing about the cylinder was measured. This figure was used as a gauge of the activity of the ointment.

The table shows the results.

*Zone of Inhibition of Penicillin Ointment Kept at Room Temperature and at Refrigeration Temperature*

| Day | Room Temperature | Refrigeration Temperature |
|-----|------------------|---------------------------|
| 1   | 2.5 cm           | 2.7 cm                    |
| 2   | 2.4 cm           | 2.5 cm                    |
| 3   | 1.25 cm          | 1.5 cm                    |
| 4   | Negative         | 2.2 cm                    |
| 5   | Negative         | 1.9 cm                    |
| 6   | Negative         | Negative                  |

To determine the sensitivity of the skin to penicillin ointment, an experiment was conducted whereby a small amount of the ointment was applied in the form of a patch test to the skin of 200 hospital corpsmen. At the end of a forty-eight hour period, observation disclosed that in not a single instance was any evidence of sensitivity displayed.

### CONCLUSIONS

Penicillin in an ointment form rapidly lost its effectiveness in inhibiting the growth of bacteria. Kept at room temperature, the ointment gave no evidence of activity after three days, kept at a refrigerator temperature of 15 C its apparent activity extended over a period of five days.

Penicillin in ointment form was relatively non-irritating to the skin.

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# DISEASES OF THE SKIN AMONG THE NATIVES OF NORTHEAST NEW GUINEA

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In New Guinea interest in dermatology has been greatly stimulated by the fact that diseases of the skin are responsible for 20 per cent of the total general admissions to hospitals as well as for a large percentage of evacuations to the United States. The reasons for this unusual prevalence are not within the scope of this paper. However, it was thought that a report on the incidence of various types of cutaneous diseases in the native population of northeast New Guinea might be of some interest and value in forming a foundation on which future studies might be based.

One thousand and forty-seven persons selected at random from a work compound and a nearby native hospital were examined. The great majority of the 260 hospital patients had been admitted because of nondermatologic medical and surgical conditions. With the exception of 15 women and 10 children the subjects were men having an age distribution comparable to that of American troops stationed in this theater.

The following is a tabulation of the results of the survey.

*Percentage of Various Cutaneous Diseases in Group Examined*

|    | Classification             | Number | Percentage |
|----|----------------------------|--------|------------|
| 1  | Normal                     | 398    | 57.0       |
| 2  | Tinea (all types)          | 200    | 19.1       |
| a  | Tinea circinata (corporis) | 67     | 6.4        |
| b  | Tinea versicolor           | 59     | 5.7        |
| c  | Tinea imbricata            | 39     | 3.7        |
| d  | Tinea cruris               | 34     | 3.2        |
| e  | Tinea of feet              | 1      | 0.1        |
| 3  | Ulcer (unclassified)       | 118    | 11.3       |
| 4  | Scabies                    | 97     | 9.3        |
| 5  | Fethyma                    | 32     | 3.0        |
| 6  | Keloid                     | 17     | 1.6        |
| 7  | Acne                       | 7      | 0.6        |
| 8  | Yaws                       | 6      | 0.5        |
| 9  | Impetigo                   | 6      | 0.5        |
| 10 | Verruca vulgaris           | 3      | 0.2        |
| 11 | Molluscum contagiosum      | 3      | 0.2        |
| 12 | Elephantiasis (filarial)   | 3      | 0.2        |
| 13 | Lipoma                     | 3      | 0.2        |
| 14 | Folliculitis               | 2      | 0.1        |
| 15 | Granuloma inguinale        | 1      | 0.1        |
| 16 | Pericoma                   | 1      | 0.1        |
| 17 | Furuncle                   | 1      | 0.1        |
| 18 | Circumscribed myxedema     | 1      | 0.1        |
| 19 | Varicose ulcer             | 1      | 0.1        |
| 20 | Cellulitis                 | 1      | 0.1        |

In the group examined, two concurrent dermatologic diseases were found in 48 natives, and

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three coexistent diseases were found in each of 4 subjects.

It might be of some interest to record a few personal observations concerning this series of cases.

## PERSONAL OBSERVATIONS BY AUTHOR

**Ulcers** Ulcers of varying sizes and shapes were frequently encountered (11.3 per cent), the chief sites being the ankles and lower third of the legs. No attempt was made to determine the exact cause in each case, but it was thought that the largest number was due to injury followed by secondary infection of the wound. A few, however, may have been manifestations of yaws or leishmaniasis. Some of the ulcers exhibited a dirty membranous base in which one would consider the possibility of involvement with diphtheria bacilli, a disease not uncommon in this region. In many cases in which no ulcers were present the end results of former lesions were visible in the form of atrophic depigmented scars.

**Scabies** This disease, termed kass-kass by the natives, was a common finding (9.3 per cent), and differs in no way from the infestation seen in the temperate zone.

**Fungus Disease** *Tinea circinata* (corporis) was characterized by large annular lesions, some of which measured 20 cm in diameter. Their advancing margin was frequently infiltrated, but there was no tendency toward residual scarring or atrophy.

*Tinea imbricata*, called gre-le by the natives, is nonexistent in the temperate zone but was common in this region. Its appearance was characteristic since it created bizarre and picturesque markings of an intricate nature over the entire cutaneous envelope. It is said that despite the intense itching many natives prefer not to be treated, since they feel that the symmetric whorled pattern produced by this eruption is a mark of distinction.

*Tinea versicolor* was always associated with partial depigmentation. This finding would tend to substantiate the belief that the pigmentary

disturbance is due to some factor inherent in *Microsporon furfur* rather than to its filtering effect on solar radiation

*Tinea of the feet* was extremely uncommon, since only one example of interdigital dermatophytosis was encountered in this survey. This may be explained by the fact that the natives do not employ footwear of any type, their feet are wide with the toes spread apart, as a result of which there is no maceration of the skin in the interdigital spaces

*Tinea of the scalp or nails* was not observed

*Yaws*—Only 6 cases of yaws were encountered. All of these were in children. The nodular granulating raspberry-like lesions were characteristic and did not present a diagnostic problem. However, yaws is undoubtedly much more prevalent than this survey would seem to indicate. Since reactions to the serologic tests (Kahn, Kline, Wassermann) are almost universally positive in the native populace, asymptomatic yaws would be extremely difficult, if not impossible to diagnose. A number of cases reported here as cases of unclassified ulcers might well have been late yaws

*Keloid*—In view of the prevalence of this entity in the American Negro, one would expect that the finding of hypertrophic scar tissue might be decidedly common in natives of New Guinea. This expectation would be heightened by the fact that numerous scars produced by trauma, accidental and self-induced (tattooing, multiple incisions for symptomatic relief of painful conditions), are seen in almost every native. However, pendulous overgrowths were not encountered and even small keloids were only occasionally noted (1.6 per cent)

*Verruca Vulgaris*—Warts were remarkably infrequent among the natives as compared with their high incidence among United States Army personnel

*Elephantiasis*—In the 3 cases observed swelling was limited to one lower extremity. However, subclinical filariasis is thought to be practically universal, as manifested by transitory attacks of edema and the presence of masses of enlarged painless femoral lymph nodes which

are seen in an overwhelming proportion of the adult male natives

*Vitamin Deficiency*—As a whole the native were a well nourished group, and in spite of a rather limited diet showed no cutaneous signs of vitamin deficiency

*Mouth Lesions*—Since most of the natives are inveterate chewers of betel nut, the buccal mucosa was examined in 500 cases. No instances of leukoplakia or epitheliomatous changes were found. Except for an orange red stain due to betel nut their teeth were in excellent condition

*Miscellaneous Findings*—One example of circumscribed myxedema involving the lower third of the right leg was seen, associated with hyperthyroidism

An extensive case of granuloma inguinale involving the axillas, postauricular folds and genitals was seen in a native woman, aged 35

Insect bites, due particularly to the sand fly were extremely common

Alopecia was rarely observed. There were no examples of alopecia areata, and only a few natives exhibited a tendency to baldness

Nevi of all types were uncommon and epitheliomas were not observed

Varicose veins were not uncommon in even the lower age group

Keratoma plantare sulcatum, characterized by punched-out circular and linear lesions scattered over the soles and associated with decided hyperkeratosis, was found to be almost universal in this area

#### SUMMARY

1 The dermatologic abnormalities in a group of 1,047 natives of northeast New Guinea are tabulated and discussed briefly

2 The most frequently encountered cutaneous diseases were scabies, ulcers and tinea, these comprised 80 per cent of all diseases of the skin noted

3 With the exception of yaws, tinea imbricata, filariasis and keratoma plantare sulcatum, the type of cutaneous disease found among the natives differs little from that seen in the United States

# SENSITIVITY OF THE TUBERCULIN PATCH TEST (VOLLMER-LEDERLE) RESULTS WITH THREE HUNDRED AND EIGHTEEN PERSONS PRESENTING VARIOUS DERMATOSES

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In 1908 Lautier,<sup>1</sup> and independently Moro,<sup>2</sup> conceived the idea of using tuberculin for testing by placing the test material on the skin without disrupting its structure. The term percutaneous was introduced to designate this method of testing the effect of materials on the skin, in contrast with von Pirquet's method and other intracutaneous and subcutaneous methods which involve traumatization of the skin.

The method of percutaneous testing with tuberculin was studied and modified in various ways by Kasahara, Wegerer, Blumenau, Habetin and Malmberg and Fromm.<sup>3</sup>

In 1933 a percutaneous tuberculin test was introduced in this country by Grozin<sup>4</sup>; he suggested the name "tuberculin patch test." Vollmer<sup>5</sup> in 1937 improved the method by saturating filter paper with undiluted tuberculin and placing it on adhesive tape. Its use and technic were further simplified by commercial mass production and distribution through the Lederle Laboratories.

While an extensive literature on the subject generally assigns to the tuberculin patch test

especially the Vollmer-Lederle material a value inferior to that of the Mantoux test, it is held to be sufficiently reliable for use in medical practice.<sup>6</sup>

Few dermatologists have published their results with the test. Kelvin<sup>7</sup> in 1941 and I<sup>8</sup> in 1943 reported on its use concomitantly with the Mantoux test without appraising its relative value. Sulzberger and Pascher<sup>9</sup> in 1944 tested 200 persons and found a high degree of correlation between the patch test and the Mantoux test performed with old tuberculin. There was 85 per cent agreement between the results obtained with undiluted old tuberculin percutaneously applied and 0.1 mg old tuberculin injected intracutaneously as well as 92 per cent agreement between the tuberculin patch test (Vollmer-Lederle) and tests with 0.02 mg old tuberculin injected intracutaneously.

While in dermatology the case-detecting value of the tuberculin tests is of secondary importance, the degree of sensitivity to tuberculin or its absence, in the presence of tuberculous lesions of the skin, is considered a criterion for the differentiation of the numerous tuberculodermas.<sup>10</sup> Studies with quantitative tuberculin patch tests have been made by Furcolow and Robinson.<sup>11</sup>

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(Footnote continued on next page)

They compared the results obtained with different concentrations of old tuberculin and of purified protein derivative of the tubercle bacillus (known as P P D ) in the patch test with the results obtained in the same person when serial dilutions of the same materials were intracutaneously injected. They found that the sensitivity to the patch test paralleled that to the Mantoux test, and that the percentage of positive reactors to the patch test was higher with the more potent material. Vollmer<sup>12</sup> determined the degree of sensitivity to tuberculin by the use of five different dilutions of tuberculin on a single strip of adhesive tape. He also found that the higher the degree of sensitivity to tuberculin the shorter was the time necessary to produce a reaction to the tuberculin patch test<sup>13</sup>. However, attempts at elaborating a quantitative method were not systematically planned.

In the present paper is set forth a comparison of the results obtained in an unselected group of dermatoses by the use of the Vollmer patch test and the intradermal tuberculin test, with the object of determining the degree of sensitivity of the patch test.

MATERIALS AND METHODS

From December 1941 until March 1944 318 patients of the dermatologic clinic of the Outpatient Department of the Long Island College Hospital were selected for the present study. These persons had various diseases of the skin as follows: acne vulgaris 148, superficial dermatomycoses 146, contact dermatitis 28, seborrheic dermatitis 14, pyoderma 12, psoriasis 8, alopecia areata 8, atopic dermatitis 6, sycosis vulgaris 6, scabies 4, urticaria 4, lichen planus 4, herpes simplex 4, hemostatic dermatitis 2, chronic folliculitis of the scalp 2, common warts 2, vitiligo 2, ichthyosis 2, erythema multiforme 2, ulcers of the legs 2, acne varioliformis 2 and para-psoriasis 2. 8 had various tuberculodermas. The group of patients was drawn entirely from the lower economic brackets and comprised approximately equal numbers of both sexes. In order to detect a possible relationship between the nature of the reaction to the patch test and the age of the subject the material was divided into ten year age groups as follows: 1 through 10 years 2 persons, 11 through 20 years 174 persons, 21 through 30 years 72 persons, 31 through 40 years 48 persons, 41 through 50 years 10 persons, 51 through 60 years 8 persons and 61 through 70 years 4 persons. The youngest person was 3 years and the oldest 70 years.

Efficiency of a Quantitative Patch Test in Detecting Reactors to Low Doses of Tuberculin, *Pub Health Rep* 56 2405, 1941

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Each subject was tested both intradermally and percutaneously. For the former old tuberculin, human (Lilly), was employed in 0.1 cc quantities in the following dilutions: 1 in 10, 1 in 100, 1 in 1,000, 1 in 10,000, 1 in 100,000, and 1 in 1,000,000. Injections were made with 1 cc of tuberculin syringes and 26 gage needles. The Vollmer-Lederle patch test was used for percutaneous testing. It was employed in the form in which it is available commercially, namely as three pieces of filter paper each measuring 1 by 1 cm and attached to a strip of adhesive tape. Two of the pieces are identical and have been saturated with undiluted tuberculin and the third, the control, with the same culture medium as that used in the preparation of the tuberculin.

Intradermal tests were performed on the flexor aspects of the forearms, and the percutaneous tests on a non-hairy part of the chest or back, after cleansing with acetone. The patch test materials were allowed to remain in position for forty-eight hours and then removed. Reactions to the intradermal tests were read forty-eight hours after the performance of the tests. Responses to the patch tests were read forty-eight hours after the removal of the materials. The sites of the tests were inspected at intervals of a few days for the appearance of delayed reactions. The smallest reaction to the intradermal test to be regarded as positive was an indurated erythematous area 5 mm in diameter. The nature of the positive response to the percutaneous test varied among the subjects tested, being erythematous, papular, papulovesicular or pustular.

RESULTS

Of 156 subjects who reacted to the Mantoux test, a dilution of 1:1,000 being used, 132, or 84.6 per cent, responded also to the patch test. The 162 persons who failed to react to the Mantoux test failed also to respond to the patch test and were further tested intradermally with 0.1 cc of dilutions of 1:100 and 1:10 of old tuberculin. The latter containing 10 mg of old tuberculin.

TABLE 1—Reactions in the Same Persons to Intradermal and Percutaneous Tests with Tuberculin

| Intradermal Test  |  | Patch Test   | Percentage of<br>Persons Yielding<br>Positive Intradermal<br>Reactions Who<br>also Gave Positive<br>Percutaneous<br>Reactions |
|---|--|--|---|
| Highest<br>Dilution<br>Yielding<br>Positive<br>Reaction | Number of<br>Persons<br>Yielding<br>Positive<br>Reaction | Number of<br>Persons<br>Yielding<br>Positive<br>Reaction |   |
| 1 in 1,000,000  | 12   | 12   | 100 0   |
| 1 in 100,000  | 36   | 36   | 100 0   |
| 1 in 10,000   | 90   | 78   | 86 7  |
| 1 in 1,000  | 18   | 6  | 33 3  |
| 1 in 100  | 16   | 0  | 0 0   |
| 1 in 10   | 24   | 0  | 0 0   |

is regarded as the largest amount of that material which can be injected with safety into healthy, nontuberculous persons<sup>14</sup>. The sensitivity of the patch test was next determined by noting the highest dilution of old tuberculin producing a positive reaction in the Mantoux test in persons who gave a positive percutaneous reaction. The results are set forth in table 1.

14 Sutherland, H. The Tuberculin Handbook, New York, Oxford University Press, 1936.

It has been claimed by Taylor, Anzen, Brock and Schnatz<sup>15</sup> that positive reactions to the patch test appear with less frequency in older than in younger age groups. On subjecting the material of this study to analysis with this point in view the results summarized in table 2 were obtained.

TABLE 2—Reactions, by Age Groups, to Patch Tests and Intradermal Tests with Old Tuberculin in the Same Persons

| Age Group,<br>Years | Total<br>Tested | Persons Yielding Positive          |             |                          |             |
|---------------------|-----------------|------------------------------------|-------------|--------------------------|-------------|
|                     |                 | Intradermal<br>Reaction<br>1:1,000 |             | Percutaneous<br>Reaction |             |
|                     |                 | Num-<br>ber                        | Per<br>Cent | Num-<br>ber              | Per<br>Cent |
| 11 through 20       | 174             | 50                                 | 28.7        | 10                       | 23.0        |
| 21 through 30       | 72              | 40                                 | 55.5        | 34                       | 47.2        |
| 31 through 40       | 48              | 42                                 | 87.5        | 38                       | 79.2        |
| 41 through 50       | 10              | 10                                 | 100.0       | 10                       | 100.0       |

COMMENT

The tuberculin patch test is equal in sensitivity to the intradermal test in persons who give positive reactions to the intradermal injection of 0.001 mg. or less of old tuberculin, that is, in highly sensitive persons. Persons who failed to react to the patch test gave positive reactions to

15 (a) Anzen, G. Efficiency of the Tuberculin Patch Test, Svenska lak-tidning 34:733, 1937, abstracted, Am J Dis Child 56:190 (July) 1938. (b) Taylor, G. Tuberculin Patch Test: A Comparison with the Mantoux Intracutaneous Test, Am Rev Tuberc 40:236, 1939. (c) Brock, H. J., and Schnatz, F. T. A Comparison of the Tuberculin Patch Test with the Mantoux Test, New York State J Med 42:1241, 1942.

intradermal injections of 0.01 mg. or more of old tuberculin. The discrepancy between the results of the two tests increases as the sensitivity of the individual decreases.

As the amount of old tuberculin commonly employed for the detection of tuberculosis by intradermal test is as high as 0.1 mg. of old tuberculin, it follows that the patch test is an inadequate measure for the routine testing of an unselected group for tuberculosis. However, should it be desired to employ the patch test for "screening" purposes, it would be necessary in the interest of accuracy to perform intradermal tests, using 0.01 mg. of old tuberculin and more, on all who failed to react to the patch test.

There is no diminution in sensitivity of the patch test in comparison to the intradermal test with an increase in age of three decades, commencing in the second, in fact, the results show a slight increase in favor of the patch test.

SUMMARY

Three hundred and eighteen persons with various diseases of the skin were tested intracutaneously with serial dilutions of old tuberculin and concomitantly with the Vollmer-Lederle tuberculin patch test material.

Analysis of the apparently high total agreement between the results obtained with both methods reveals that the Vollmer-Lederle patch test does not possess a high degree of sensitivity and is the equal of the Mantoux test only in persons highly sensitive to tuberculin. Those who fail to respond to the Vollmer-Lederle material should be retested with intradermal injections of not less than 0.01 mg. of old tuberculin.

# EFFECT OF FEEDING A LIPOTROPIC SUBSTANCE TO PATIENTS WITH XANTHELASMA

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The association of hyperlipemia with xanthelasma is well known and has been the subject of study by several investigators<sup>1</sup> The relation which the hyperlipemia has to cardiovascular disease, especially peripheral and coronary arteriosclerosis, is less well recognized but likewise has been found to be rather common<sup>1</sup> From such observations, it would seem that the presence of these benign fatty lesions within the skin of the eyelids may suggest a disturbance in fat metabolism, in some persons severe enough to warrant further study in regard to the blood lipids, cardiac function and peripheral vascular sufficiency

If xanthelasma may at times be the herald lesions of disturbed fat metabolism, it then should be determined whether some of the lipotropic substances which have so pronounced an effect on several types of experimental and acquired disturbances in fat storage and metabolism might not be of value in lowering the blood fat levels and possibly, because of these changes, in causing an absorption of the local lesions

Studies and contributions from the Department of Dermatology and Syphilology of the University of Michigan Medical School, service of Dr Udo J Wile and Dr Arthur C Curtis

1 Muller, C Xanthomata, Hypercholesteremia, Angina Pectoris, Acta med Scandinav, 1938, supp 89, pp 75-84 Montgomery, H, and Osterberg, A E Xanthomatosis Correlation of Clinical Histopathologic and Chemical Studies of Cutaneous Xanthoma, Arch Dermat & Syph **37** 373-402 (March) 1938 Montgomery, H Cutaneous Xanthomatosis, Ann Int Med **13** 671-676 (Oct) 1939, Cutaneous Manifestations of Diseases of Lipoid Metabolism, M Clin North America **24** 1249-1269 (July) 1940 Thannhauser, S J, and Magendantz, H Difficult Clinical Groups of Xanthomatous Diseases Clinical Physiological Study of Twenty-Two Cases, Ann Int Med **11** 1662-1746 (March) 1938 Polano, M K Xanthomatosis of the Skin, Arch f Dermat u Syph **181** 139-179, 1940, abstracted, Wise, F, and Sulzberger M B Yearbook of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc, 1941, pp 208-211

With these theoretic possibilities in mind, we have conducted some experiments, using one related group of lipotropic substances, on a series of patients with xanthelasma

## PROCEDURE AND METHODS

In this study, the total fasting blood lipids of 18 normal hospital employees, the total fasting cholesterol of 10 members and the fasting free cholesterol of 9 members each of this group were used as our controls

The total fasting blood lipids of 39 patients with xanthelasma were determined and compared with those of the controls For 26 of these patients, determinations of fasting total and free blood serum cholesterol were made and compared with the normal For 17 patients, determinations of the fasting total blood phospholipids were also made When more than one fasting blood specimen was drawn, the average of all determinations was taken

Eight patients were studied before and during the feeding of the lipotropic substance Fasting blood was drawn at intervals of seven days throughout the experimental period This group had 134 separate determinations each of the fasting total lipids and free and total cholesterol and 122 separate determinations of the fasting phospholipids The experimental interval ranged from 46 to 189 days (46, 63, 69, 98, 126, 150, 160 and 189 days) After preexperimental analyses of fasting blood lipids each patient was advised to ingest soybean lecithin complex in the form of 5 Levo wafers<sup>2</sup> daily, divided as desired The diet was not controlled

2 The wafers were supplied by the American Lecithin Company Inc, Elmhurst, Long Island, N Y The analysis of the wafers is given as follows

| Average weight per wafer                 | 16 85 Gm |    |           |
|--|----------|----|-----------|
| Composition                              | Per Cent | Gm | per Wafer |
| Moisture                                 | 6 88     |    | 1 18      |
| Mineral matter                           | 2 44     |    | 0 41      |
| Fat                                      | 14 92    |    | 2 52      |
| Soybean lecithin (lipid P $\times$ 47 6) | 18 24    |    | 3 07      |
| Protein (protein N $\times$ 5 7)         | 5 04     |    | 0 85      |
| Carbohydrates (by difference)            | 52 48    |    | 8 82      |
|  | 100 00   |    | 16 85     |
| Calories per wafer (16 85 Gm)            | 89       |    |           |

The soybean lecithin in the analysis refers to the lecithin complex, which consists of approximately equal parts of lecithin, cephalin and lipositol (inositol phosphate)

Each patient ingested daily 15.35 Gm of soybean lecithin, or, according to analysis, approximately 5 Gm each per day of lecithin, cephalin and inositol. Hereafter, this complex will be called the lipotropic substance.

No definite evidence of intolerance to the lipotropic substance was noted. No more than the usual fluctuation of weight was observed in any patient.

The analysis of the lipids was carried out on aliquot portions of a stock extract prepared by refluxing serum with ether-alcohol, filtering off the precipitate of serum proteins and refluxing the precipitate again, first with absolute alcohol and then with absolute ether. The combined extracts, after concentration by vacuum distillation, were then taken up in purified petroleum

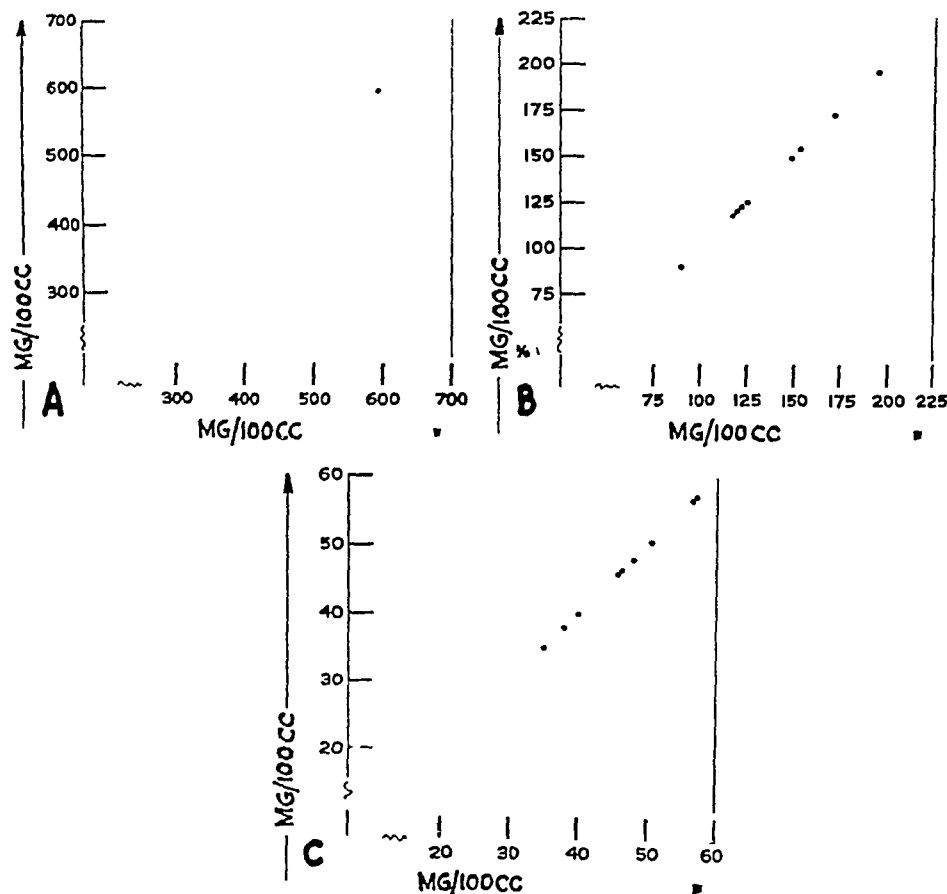


Chart 1—The range of total fasting blood lipids (A), total fasting blood serum cholesterol (B) and fasting free blood serum cholesterol (C) is shown for 18, 10 and 9 normal persons.

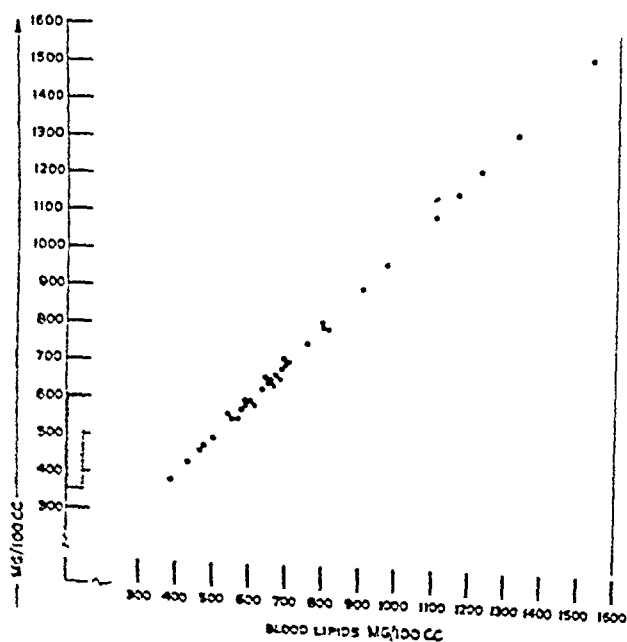


Chart 2—The total fasting blood serum lipids in 39 patients with xanthelasma are shown, compared with the range of the same blood fats in 18 normal persons (indicated by cross-hatched rectangle). It can be seen that some patients with xanthelasma have severe degrees of lipemia.

benzene, washed with water, dried with anhydrous sodium sulfate and finally made up to volume.

Total lipids were determined gravimetrically by the method of Bloor<sup>3</sup>. The simpler alternative oxidative method was not used because (1) oxidation is incomplete in varying degree, (2) other substances present, in addition to lipids, are oxidizable and (3) all such determinations are much magnified by a micromethod.

Determinations of the total and free cholesterol were carried out by the modified colorimetric method of Shoenheimer and Sperry<sup>4</sup>. The usual colorimetric method is not specific because of the presence of interfering substances which also produce color. The digitonin method was used for this study because it yields cholesterol only, and the photoelectric colorimetric reading on the solution of digitonin precipitate is micro-specific.

<sup>3</sup> Bloor, W. R. Determination of Small Amounts of Lipid in Blood Plasma, *J. Biol. Chem.* **77** 53-73 (April) 1938.

<sup>4</sup> Shoenheimer, R., and Sperry, W. M. Micro-method for Determination of Free and Combined Cholesterol, *J. Biol. Chem.* **106** 745-760 (Sept) 1934.



Total phospholipids were determined by a combination of Bloor's precipitation method<sup>5</sup> and the phosphorus method of Fiske and Subbarow.<sup>6</sup> The phosphorus method of Fiske and Subbarow is the most accurate for the determination of the phospholipids and lends itself best to photoelectric colorimetry. It may be criticized because with acetone precipitation the yield is only 85 to 90 per cent. However, it is the only method applicable at present for routine analysis of serum phospholipids.

#### DATA AND COMMENT

Chart 1 shows that the total fasting blood lipids of the normal persons range from 360 to 600 mg the total cholesterol from 90 to 171 mg

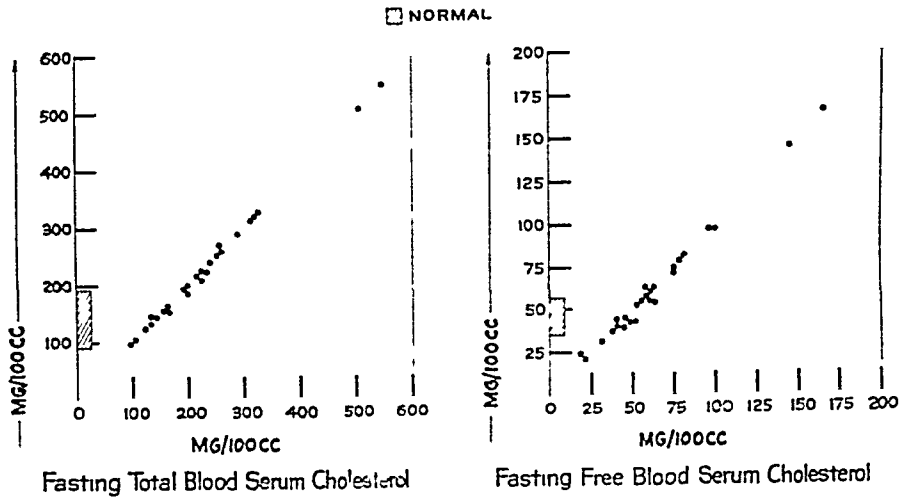


Chart 3—The fasting total and free blood serum cholesterol of 26 patients with xanthelasma is shown, compared with our normal levels. The increase of both of these substances in many of the patients is apparent.

and the free cholesterol from 38 to 57 mg per hundred cubic centimeters.

Of 39 patients with xanthelasma the total fasting blood lipids were above these levels in 26 or 66 per cent (chart 2). In 7 patients, more than 1 per cent of the blood was fat. The fasting blood cholesterol was abnormally high in 15 or 57.7 per cent and of the same 26 patients 11 or 42.3 per cent had high fasting free blood cholesterol values (chart 3). Seventeen of these patients had fasting blood phospholipids which were abnormal according to accepted normal levels (chart 4).

Eight patients followed during the ingestion of the lipotropic substance for forty-six to one hun-

dred and eighty-nine days showed relatively little change in the fasting total blood lipid levels for nearly one hundred days (chart 5). The largest number of determinations are in this part of the curve. When the number of the subjects and the number of determinations decrease, the curve begins to fluctuate because of individual variations dominating its character and it loses its statistical value. We believe one can say that for the time these patients were observed the lipotropic substances fed had no apparent effect on the total blood fat values. The curves for total and free cholesterol are almost a straight

line (chart 6) and hence were not affected by feeding of the lipotropic substance. Likewise,

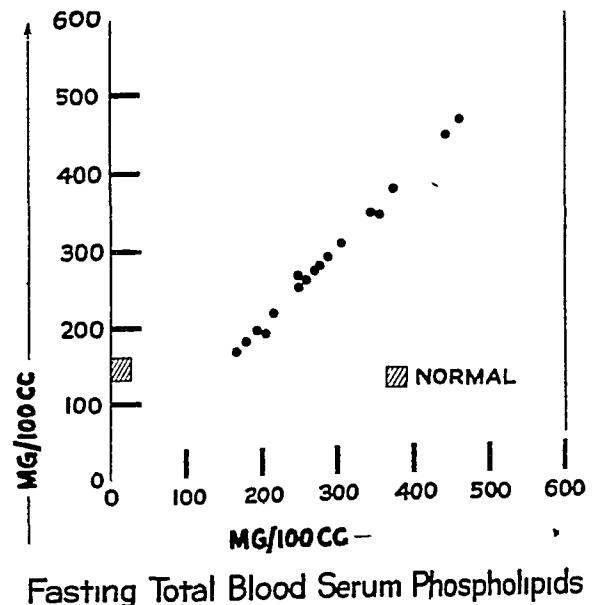


Chart 4—The total blood serum phospholipid levels of 17 patients having xanthelasma are shown. All determinations are abnormally elevated.

5 Bloor, W. R. Oxidative Determination of Phospholipid (Lecithin and Cephalin) in Blood and Tissues, *J Biol Chem* **82** 273-286 (May) 1929.

6 Fiske, C. H., and Subbarow, Y. Colorimetric Determination of Phosphorus, *J Biol Chem* **66** 375-400 (Dec) 1925.

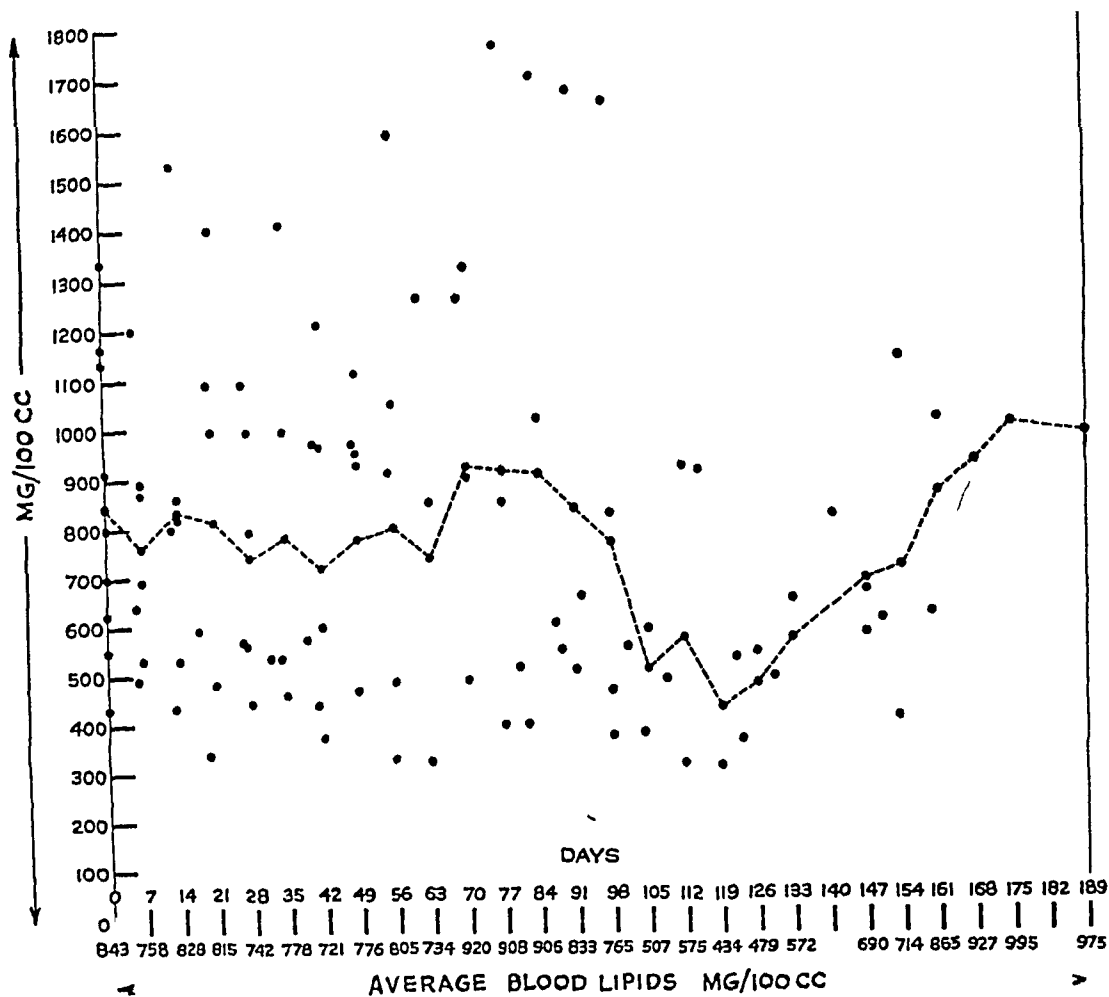


Chart 5—Individual determinations, plotted in a scatter curve, of the total fasting blood serum lipids of 18 patients followed for as short a period as forty-six days and as long as one hundred and eighty-nine days are shown. There is no appreciable change in the fat levels until the period of one hundred days is reached. After this time, the number of values is too few for prediction of any statistical trend.

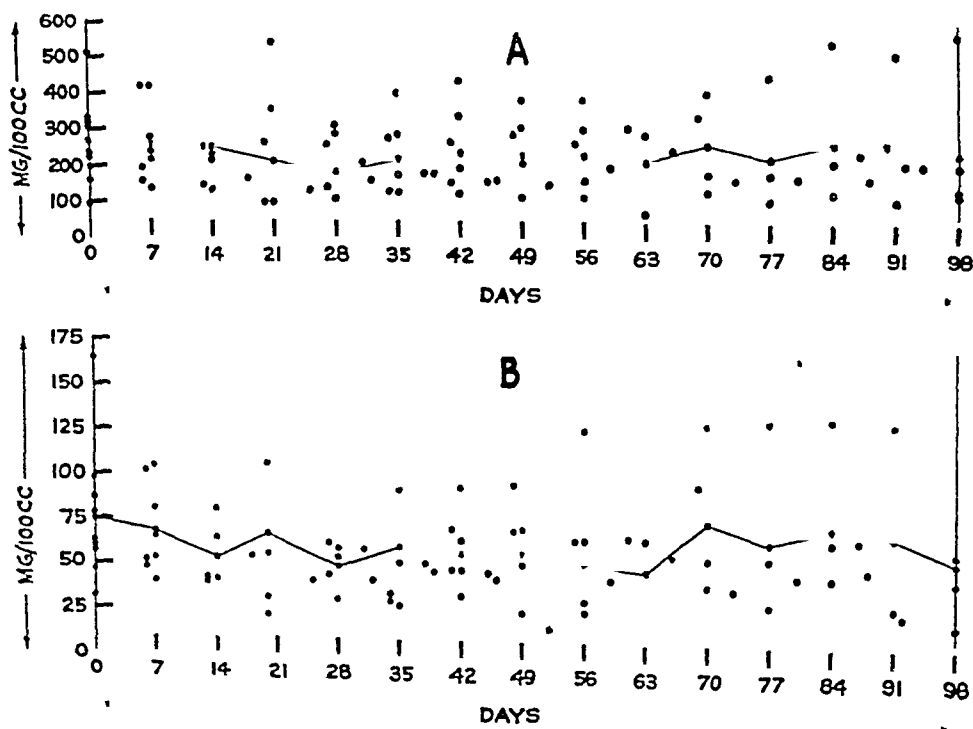


Chart 6—The total (A) and free (B) blood serum cholesterol values for 8 patients having xanthelasma who were daily ingesting a lipotropic substance is shown in the two charts. The straight line average in both instances shows that the substance had no effect on either type of blood cholesterol.

there was no consistent change in the total blood phospholipids (chart 7)

From the clinical standpoint, only 1 patient presented changes in the lesions during the period of lipotropic feeding. She had a fasting total blood lipid level of 1,170 mg per hundred cubic centimeters, a total cholesterol level of 325 mg, a free cholesterol level of 97.5 mg and a total phospholipid level of 303 mg. After sixty-three days of ingestion of the lipotropic substance, her xanthelasma lesions entirely disappeared, although all blood lipid fractions were

unless the disappearance of the lesions in the single patient can be attributed to the lecithin complex

CONCLUSIONS

1 In a series of 39 patients with xanthelasma, 66 per cent were found to have abnormally high fasting total blood fats. Fifty-eight per cent of 26 patients had abnormally high total blood serum cholesterol and 42 per cent of 26 patients had abnormally high free blood serum cholesterol. All phospholipid determinations were above the accepted normal level.

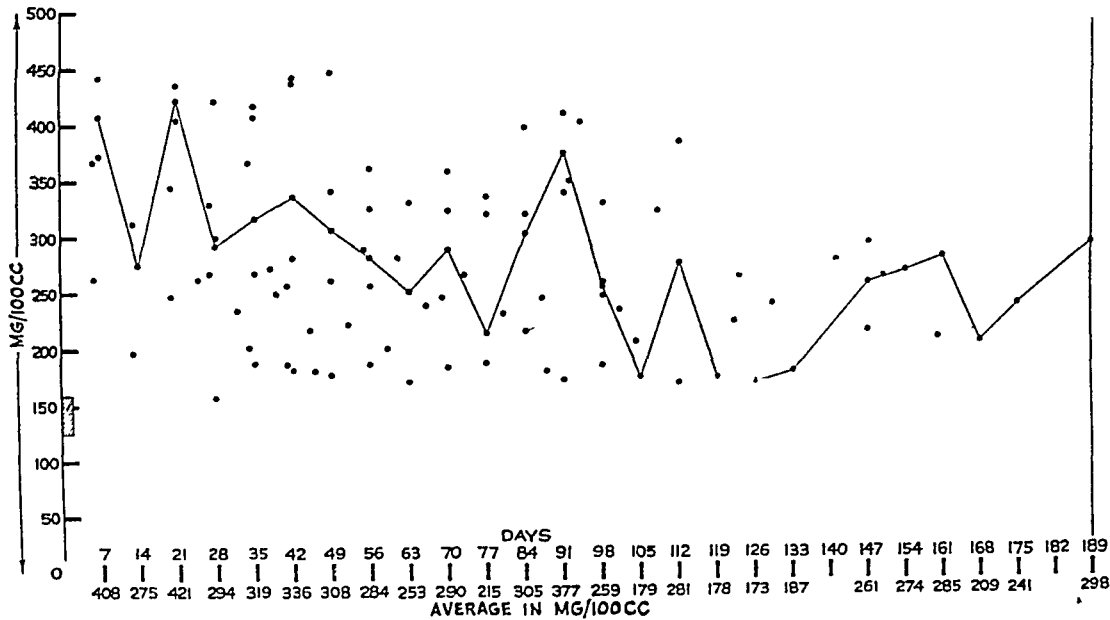


Chart 7—The total blood serum phospholipids determined for 8 patients having xanthelasma who were ingesting a lipotropic substance daily is shown as a scatter curve. The solid line represents averages. Again no important deviation in the phospholipids is apparent.

not significantly changed. This isolated case may or may not be an example of spontaneous regression of the lesions.

A criticism of our experiments might arise from the fact that we gave only 15 Gm. of lecithin complex daily. This amount was empirically used, but we believe it was enough to show a trend in this disease had the substance been effective.

It is apparent from this study that the lipotropic substance used had no effect on blood lipids and none on the xanthelasma lesions.

2 Soybean lecithin complex, containing approximately 5 Gm. each of lecithin, cephalin and inositol, fed daily to 8 patients for a period ranging from forty-six to one hundred and eighty-nine days, had no significant effect on the blood lipids or the cutaneous lesions. The disease in 1 patient cleared without change in the blood fats. This is interpreted as a spontaneous resolution.

3 Increased dosages and different lipotropic substances might be a subject for further experimental study on xanthelasma.

# RELATION OF ULTRAVIOLET-INDUCED MUTATIONS TO SPECIATION IN DERMATOPHYTES

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Variability of a sort not susceptible to genetic analysis is a frequently observed phenomenon among fungi and bacteria<sup>1</sup> and is an important interfering factor in the recognition and identification of pathogenic fungi. It is important from the standpoint of any systematic study that the permanence, frequency and extent of such variation be known. In the case of some fungi, mutants have been subjected to genetic analysis.<sup>2</sup> The sudden appearance, diversity and permanence of the type of variation under discussion and the genetic behavior of analogous variants in neurospora and in yeasts seem to justify the designation "mutant" for these variants. The published report<sup>3</sup> of a series of remarkable mutations appearing spontaneously in an old culture of the pathogenic fungus *Microsporon gypsum* concluded with the hypothesis, "many of the dermatophytes now known as species are only varieties of a single unstable species."<sup>4</sup> The conclusions reached at that time, the frequent observation of variation in dermatophytes,<sup>5</sup> the many published descriptions of "new" species of pathogenic fungi and the difficulties of evaluating

species and of identifying the occasional aberrant strains encountered have been in part responsible for our interest in induced mutations in these fungi.

In an investigation of the fungicidal action of monochromatic ultraviolet radiation we<sup>6</sup> have observed, among other sublethal effects of radiation, a stimulation of variability. Under carefully controlled conditions of appropriate wavelength and exposure it was shown that when a suitable strain of *Trichophyton mentagrophytes* was irradiated as many as 40 per cent of the surviving conidia yielded mutants. The rate of mutant production rose to a maximum on application of energy (monochromatic ultraviolet radiation, 2,650 angstrom units) of the order of 0.01 erg per spore and decreased when the energy (time of exposure) was further increased. Representative mutants from that series have now been carried in cultures for five years (about twenty transfers) and they still exhibit their distinctive characteristics. In this and subsequent studies<sup>7</sup> several hundred mutants have been isolated.

Conclusive evidence that these forms were actually mutants and not air-borne contaminants was presented in the earlier paper and can be summarized here as follows. No mutants appeared in the controls, 5,000 nonirradiated conidia being subcultured in order to test this point. It was again demonstrated, however, that when subcultures are made from old cultures of *Trichophyton*, mutants, similar in some cases to the types induced, appear spontaneously. It

6 Hollaender, A, and Emmons, C W. The Action of Ultraviolet Radiation on Dermatophytes. I. The Fungicidal Effect of Monochromatic Ultraviolet Radiation on the Spores of *Trichophyton mentagrophytes*, *J Cell & Comp Physiol* **13** 391-402, 1939. Emmons, C W, and Hollaender, A. The Action of Ultraviolet Radiation on Dermatophytes. II. Mutations Induced in Cultures of Dermatophytes by Exposure of Spores to Monochromatic Ultraviolet Radiation, *Am J Botan* **26** 467-475, 1939.

7 Hollaender, A, and Emmons, C W. Wavelength Dependence of Mutation Production in the Ultraviolet with Special Emphasis on Fungi, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L I, New York, The Biological Laboratory, 1941, vol 9, pp 179-186.

From the Division of Infectious Diseases and the Industrial Hygiene Research Laboratory, National Institute of Health, United States Public Health Service, Bethesda Md

1 Brierly, W B. Variation in Fungi and Bacteria, *Proc Internat Cong Plant Sc* **2** 1629-1654, 1929. Chilton, S J P. Variations in Sporulation of Different Isolates of *Colletotrichum destructivum*, *Mycologia* **35** 13-20 1943.

2 Dodge, B O. Breeding Albinistic Strains of the *Monilia* Bread Mold, *Mycologia* **22** 9-38, 1930. Winge, O. On Haplophase and Diplophase in Some *Saccharomycetes*, *Compt rend d trav du lab Carlsberg, serie physiol* **21** 77-111, 1935. Lindegren, C C, and Lindegren, G. The Use of the Fungi in Modern Genetical Analysis, *Iowa State Coll J Sc* **16** 271-290, 1942.

3 Emmons, C W. Pleomorphism and Variation in the Dermatophytes, *Arch Dermat & Syph* **25** 987-1001 (June) 1932.

4 Use of the term "species" in mycology is based on morphologic concepts. The application of genetic standards to definition and delimitation of species of fungi is impossible or impractical in most cases.

5 Neal, P A and Emmons, C W. Dermatitis and Coexisting Fungous Infections Among Plate Printers, Bulletin 246 United States Treasury Department Public Health Service 1939, pp 1-55.

was concluded that the radiation accelerated an inherent tendency to mutation production. In about half the irradiation experiments ordinary plating methods were used to insure purity of the strain. In the remaining half the progeny of a single conidium were irradiated. In both cases conidia not exposed to radiation invariably yielded colonies like the parent strain, but among the conidia surviving radiation many produced new types of colonies. The percentage of these mutants varied with the wavelength used and the amount of energy applied. The occurrence of as many as 40 per cent of mutants among survivors in some runs and their complete absence from control runs rule out the possibility of a heterogeneous population in suspensions of conidia used. An examination of the mutants showed that they were not ordinary air-borne contaminants. Their morphologic characteristics were clearly those of dermatophytes. The conidia and macroconidia were those of *Trichophyton*, although abnormal in size or shape in some instances. In most cases the mutants retained their pathogenicity for animals, which conclusively identified them as dermatophytes. However, dermatophytes have never appeared in this laboratory as air-borne contaminants. Further, with a few exceptions to be noted later, these mutants presented characteristics which were not possessed by other dermatophytes carried in the laboratory. In fact, the majority of the mutants were easily distinguishable from all known species of fungi.

It is the purpose of this report to emphasize the permanence of these mutants which have been kept in culture five years, to point out in more detail the similarities between certain mutants induced by ultraviolet radiation in the studies cited and certain "species" usually considered distinct and to discuss the taxonomic implications associated therewith.

The fungus exposed to monochromatic ultraviolet radiation in these experimental studies was a variety of *T. mentagrophytes* resembling that described by Sabouraud as *Trichophyton gypsumi asteroides* (fig 1). It produces on acid dextrose agar (Sabouraud's)<sup>8</sup> a flat, spreading colony, the aerial hyphae being light buff or cream colored at the center to white toward the periphery and overlying reddish brown hyphae growing in the substratum. The surface was granular, owing to the production of innumerable clusters and aggregations of conidia. Many of the conidia-bearing hyphae grew in strands and ridges having a radial orientation. This was

most conspicuous in the peripheral half of the colony and was responsible for the asteroid character. A reddish-brown pigment produced in the hyphae growing in the substratum was visible over almost the entire reverse of the colony. The microscopic appearance was typical of *Trichophyton*, both conidia and macroconidia as well as spiral hyphae and abortive ascogonia being produced. The conidia were one celled and subspherical, the macroconidia one to several celled and clavate.

The induced mutants derived from this fungus differed from it so widely that, according to generally accepted criteria of classification of the dermatophytes, had their origin been unknown many of them could not have been identified with it. The mutants could be grouped roughly into a number of categories and a few types appeared repeatedly, but for the most part they differed from each other and represented a wide range of variation. Some grew more rapidly than the original while most grew more slowly and some never spread widely over the substratum. Some produced more pigment than the original, and others produced less. The amount of aerial mycelium varied from a profuse cottony growth in some mutants to almost none in others. A few of these mutants which resemble other named species sufficiently to suggest a possible mutational origin for the latter will be described in detail.

#### MUTANT A

Several of the mutants (type A, fig 2) induced by ultraviolet radiation closely resembled the "species" *Trichophyton interdigitale*. They were floccose, covering most of the surface of an agar slant with a cottony mycelium, and powdery toward the center, unlike the chalky and granular surface of the original type. The greater profusion of aerial hyphae was associated with a relative decrease in production of conidia and to some extent with morphologic changes in the conidia. The conidia of the original strain were subspherical and borne in dense clusters on specialized branching conidiophores. In the mutant the conidia were subspherical or clavate and while branching conidiophores were present, there was a relative increase in the number of conidia borne on simple lateral conidiophores or directly as lateral buds from undifferentiated hyphae. With the acquisition of an exuberant cottony aerial mycelium, the mutant lost the astral or raylike character of the original strain. There was also a decrease in the amount of pigment produced in the reverse of the colony. Associated with the cultural and morphologic

8 Difco neopeptone 1 per cent, chemically pure dextrose 4 per cent, agar 2 per cent, pH 5.6



Fig 1—Original strain of *T. mentagrophytes*

Fig 2—Mutant A

Fig 3—Mutant B

Fig 4—Mutant C

Fig 5—Mutant D

Fig 6—*T. violaceum*

alterations found in this mutant, there was a slight decrease in virulence for experimentally infected animals

In all the changed characteristics enumerated the mutants of type A resemble *T. interdigitale*. The resemblance is so close that, given one of the mutants for identification, we know of no criteria, except possibly the degree of virulence, by which it could be separated from that variety.

Spontaneous variation in the species *T. mentagrophytes* is generally admitted to be considerable. Sabouraud, ignoring earlier valid names, improperly renamed this fungus *T. gypsum* and designated several varieties or subspecies which he subsequently raised to specific rank. Later studies have broadened the concept of this species so that in the opinion of many mycologists it should be emended to include *T. interdigitale*<sup>9</sup> (the fungus most commonly associated with dermatophytosis of the foot), *Trichophyton pedis*, *Trichophyton niveum* and perhaps others. We believe our experimental evidence substantiates this conception. The practical consequences of this interpretation of *T. interdigitale* will be considered later.

#### MUTANT B

In a second group of mutants the increase of aerial hyphae with concomitant decrease in sporulation had proceeded further. The aerial mycelium was white, developed rapidly and extended up onto the sides of the tube (fig 3). Conidia were clavate, borne only laterally on undifferentiated hyphae, and fewer in number than in the original. Virulence for the guinea pig was less than for the original strain, but active spreading lesions were produced. These mutants resemble *T. niveum* so closely that no differential criteria except greater virulence were found. The resemblance to the so-called pleomorphic condition which appears in old cultures of many dermatophytes should also be pointed out. This "pleomorphic" mycelium represents a type of degenerative change which appears spontaneously and from which the original type of growth cannot be recovered unless some unchanged (i.e., nonmutated) conidia remain in the tube from which the inoculum is taken. "Pleomorphism," as the term has been used in connection with the dermatophytes, is a type of permanent mutation which appears spontaneously and invariably in many species. As has been pointed out, other types of mutants also develop, but

the early appearance of the pleomorphic overgrowth and its tendency to spread over the surface of the colony obscure other less apparent and less aggressive mutants. *T. niveum* has been considered by many mycologists to be a naturally occurring mutant, and in this opinion we concur. The appearance of an induced mutant in this series which resembles *T. niveum* and the common type of pleomorphic degeneration is of interest because it supports the hypothesis that radiation accelerates a type of change which later appears spontaneously. It is surprising, however, that this type of mutant was isolated only a few times.

#### MUTANT C

The first two mutants considered may be looked on as representing degenerative changes in which there was a decrease in complexity and virulence of the original strain. In mutant C (fig 4), although there was a decrease in rate of growth, sporulation was abundant and degenerative changes were not apparent. The colony was small, with a granular chalky surface and an even margin contrasting with the raylike extensions from the margin of the original. The colony was cream colored, with a normal amount of reddish brown pigment in the reverse. Sub-spherical conidia were formed in great profusion, and the macroconidia and spiral hyphae resembled those of the original. Pathogenicity for the guinea pig was slightly less than that of the original type.

This mutant, which was isolated several times, resembles the variety which Sabouraud called *T. gypsum granulorum*. It differs from the original in slower rate of growth and absence of the radiating margin. These are insufficient differences on which to base species, and the fact that an induced mutation crosses this artificial barrier tends to support the conception of a few variable species within the genus *Trichophyton* rather than many narrowly defined species.

#### MUTANT D

About half of the mutants isolated were more deeply pigmented than the original, and some of these (fig 5) bore a superficial resemblance to *Trichophyton violaceum*. The colony developed slowly and after fourteen days was 2.5 cm in diameter. The surface was nearly glabrous and was thrown into folds, some radiating from the raised center of the colony. There was a sparse white bloom in some strains due to the production of conidia. The color was a deep reddish violet suggesting *T. violaceum*, although

<sup>9</sup> Epstein, S. Presentation of the Hypothesis that *Trichophyton Interdigitale* Is a Degenerated *Trichophyton Gypseum*, J. Invest. Dermat. 1:141-168, 1938.



the blue component of the pigment was reduced. The microscopic appearance was different from that of *T. violaceum*, many conidia and macroconidia varying greatly in size being produced. The virulence for animals was less than that of the original from which it was derived but greater than in the case of *T. violaceum* (fig 6). The mutant fungus still exhibits the ectothrix type of hair invasion, unlike *T. violaceum*, which is endothrix.

The frequency with which *T. violaceum* appears in certain geographic areas (southern Europe, northern Africa), its clinical manifestations and the distinctive characteristics of the fungus seem to justify its recognition as a separate species. However, in this country its occurrence is sporadic and the origin of the infectious agent is unknown in most cases. The possibility of a mutational origin for the species ought to be considered. It is well known that the species is variable, most strains after being carried in the laboratory losing the ability to form pigment and becoming indistinguishable from *Trichophyton glabrum*. Pigment production in all the species of *Trichophyton* is a variable character, depending on the culture medium and conditions of growth and disappearing in many cases on long-continued subculture. In the case of mutant D it is notable that there was a permanent increase in pigment production associated with loss of aerial mycelium. In both these modifications it approaches *T. violaceum*.

#### COMMENT

A high percentage of mutants (some of which approach or cross "species" lines) appeared among the progeny of conidia of *T. mentagrophytes* exposed to monochromatic ultraviolet radiation. It is suggested that this fact offers experimental evidence for a mutational origin of some varieties or species of dermatophytes. If this hypothesis is accepted, it can still be argued that the theoretic implications need not

lead to a revision of the nomenclature of these fungi, since it may seem convenient to have a specific name for each cultural type of the variable species *T. mentagrophytes*. However, the advantages of a different specific name for each variety may well be questioned. The occurrence of intermediate types in the isolates of this species is a matter of common knowledge among mycologists culturing these fungi. The intermediate characteristics and the instability of many of these strains make varietal or specific identification difficult in many cases. Further, it is well known that although there is a correlation along broad lines between the species of dermatophyte and the clinical type of lesion it produces,<sup>10</sup> this correlation does not hold in the case of varieties of *T. mentagrophytes*.<sup>11</sup> There are many observations on the variability of this and other species, and, while some of them have been interpreted to indicate a multiplicity of species, we believe that they can be more properly interpreted as mutants.

#### SUMMARY

Four types of mutants induced by monochromatic ultraviolet radiation of conidia of *Trichophyton mentagrophytes* were distinguished after they had been carried in subcultures for a period of five years. Some of these are closely similar to certain varieties of *Trichophyton* which occur naturally and are recognized as being closely related but are usually placed in different species. One mutant approaches the "endothrix" species *T. violaceum* but is not considered identical with it. These observations support the hypothesis that species lines have been drawn too narrowly among the dermatophytes and that some so-called species may have a mutational origin.

10 Sabouraud, R. *Les teignes*, Paris, Masson & Cie, 1910.

11 Dowding, E. S., and Orr, H. Three Clinical Types of Ringworm Due to *Trichophyton* Gypseum, *Brit J Dermat* 49:298-307, 1937. Epstein<sup>9</sup>

# CONTACT DERMATITIS OF EYELIDS CAUSED BY AN ANTIOXIDANT IN RUBBER FILLERS OF EYELASH CURLERS

## REPORT OF SEVEN CASES

CAPTAIN GEORGE H CURTIS

MEDICAL CORPS, ARMY OF THE UNITED STATES

Eyelash curlers are metal instruments widely used by women to make the curve of the eyelashes more pronounced. The instrument is similar to a scissors, with handles closing on a pivot, and operates on the guillotine principle (fig 1). The frame is curved to fit the contour of the eye; the proximal part of the frame has a linear slot that holds a black rubber filler or band about 3.5 cm long, 0.3 cm wide and 0.2 cm thick, which protrudes about 0.1 cm above the sides of the slot. The distal part of the frame is a thin curved "knife," which is fixed, and the rubber filler slides toward the "knife" as the handles are closed. The frame is placed close to

as several patients demonstrated, as the "knife" slides along the cutaneous surface and becomes coated with the bloom of the rubber filler, the skin comes into direct contact with both bloom and rubber.

Fox<sup>1</sup> reported a case of contact dermatitis due to the rubber in an eyelash curler. The patient had recurrent dermatitis with edema of both upper and lower lids. The deep horizontal folds of the upper lids were unaffected. Acute exacerbations continued after she had stopped using cosmetics. While she was in the hospital it was discovered that the exacerbations occurred within eight to twelve hours after she used an eyelash curler. Patch tests with the rubber band elicited positive reactions.

Odland<sup>2</sup> reported another case of dermatitis due to the rubber filler in an eyelash curler. The patient presented a recurrent dermatitis of the lids, which persisted after the use of cosmetics had been discontinued. The dermatitis was band-like and about 0.3 cm wide on the upper lids near the margins. Odland stated that he had seen a similar case a year before.

This report includes 7 cases of contact dermatitis due to the rubber filler in eyelash curlers. By patch tests, the specific allergen was identified in 5 cases.

## REPORT OF CASES

Cases 1, 2, 3 and 4 are so similar that case 2 is reported as representative. All the patients were white women.

CASE 2—The patient, aged 35, first seen on Nov 18, 1938, complained of itching dermatitis recurring at irregular intervals during the preceding year, which during the past several months had become continuous with frequent exacerbations. A long linear band of dermatitis involved each of the upper lids, and two short separated bands, each of the lower lids. The bands varied from 0.5 to 1.5 cm in length and from 0.2 to 0.4 cm in width. A narrow band of normal skin about 1 to 2 mm wide lay between the dermatitis and the

1 Fox, E. C. Dermatitis of the Eyelids Due to Rubber on Eyelash Curler, *Arch Dermat & Syph* 28:222 (Aug) 1933.

2 Odland, H. Sensitization in Eczema. Some Phases of Its Problem, *Northwest Med* 34:9 (Jan) 1935.

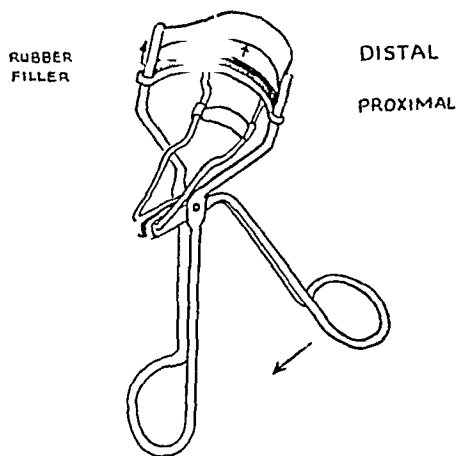


Fig 1—Eyelash curler

the surface of the upper lid, when the handles are closed, the eyelashes are clamped between the "knife" and the rubber band. Slight squeezing pressure on the handles causes the lashes to be curved sharply upward. Usually no attempt is made to curl the lower lashes, because it is difficult to manipulate the instrument upside down. An ointment supplied with the curler is applied to the lashes before curling. When the curler is applied to the eyelashes, the skin of the lid is often pinched in the guillotine, or,

From the Cleveland Clinic Foundation, Cleveland.

This investigation was completed just before I was called into service, in 1942. These instruments are probably not available at the present time.

margins of the lid. The eyelashes were artificially curled. Patch tests with the rubber filler of the curler elicited a positive reaction but with cosmetics the reactions were negative.

Case 5 is presented as representative of cases 5 and 6. Both patients were white women.

CASE 5—The patient, aged 21, first seen on Nov 30, 1938, complained of itching dermatitis characterized by frequent exacerbations at irregular intervals during the preceding month. On October 31 she had applied an eyelash dye, and the dermatitis appeared a few days later. Although she stopped using the dye, the dermatitis continued to recur. A linear band of subacute dermatitis 3 or 4 mm wide and about 2 mm above the margin of the lid involved each upper lid. Similar, but shorter, bands on the lower lids joined the bands on the upper lids just beyond the temporal canthi. The eyelashes were artificially curled. Patch tests with the rubber filler of her eyelash curler elicited positive reactions, but with cosmetics the reactions were negative.

In February 1939 she complained of a dermatitis on the dorsa of the feet of three weeks' duration. The dermatitis consisted of a central area about the size of a silver dollar, with medial and lateral rectangular extensions 1 by 1.5 cm. The lastex in her shoes conformed to the outline of the dermatitis. Patch tests with the rubber threads soaked three days in 5 per cent sodium hydroxide solution and with the cloth of the lastex gave positive results, as did patch tests with ordinary black rubber bands and a rubber filler of an eyelash curler.



Fig 2—Location of the dermatitis on the eyelids in 5 cases.

Two years later the patient presented an irregularly shaped area of dermatitis of two months' duration on the posterior surface of the left thigh. The lesion was situated at the area of contact between the skin and the rubber clamp of the hose supporter. Patch tests with the rubber of the hose supporter elicited positive

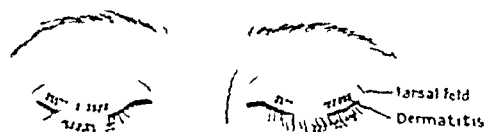


Fig 3—Location of the dermatitis on the eyelids in 5 cases.

reactions, as did patch tests with a rubber filler of an eyelash curler and a rubber band. This case has been reported in detail elsewhere.

Case 6 presented similar dermatitis of the eyelids and the posterior surfaces of the thighs.

CASE 7—A white woman, aged 30, seen on Jan 3, 1941, complained of irregularly recurring attacks of red-

ness, swelling and itching of the eyelids of six months' duration. Examination showed a well defined linear band of dry, slightly scaly, subacute dermatitis parallel to the margins of both upper and lower eyelids. The eyelashes were artificially curled. On the cheeks under the eyes were several light red, scaling papules about



Fig 4—Location of the dermatitis on the eyelids in 2 cases.

3 mm in diameter. The tenacity of the scales suggested lupus erythematosus. Patch tests with the rubber filler of her eyelash curler elicited a positive reaction, but with cosmetics the reactions were negative. The patient stopped using the curler, and at the end of two weeks the dermatitis had disappeared.

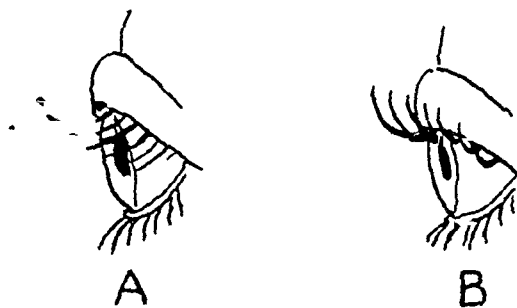


Fig 5—A, normally curved upper eyelash, B, appearance of eyelash after artificial curling.

Four months later, the lesions on the cheeks had greatly enlarged and were typical of lupus erythematosus. Similar lesions were found in the scalp. After six months' treatment with bismuth subsalicylate and gold sodium thiosulfate, the lesions healed and had not recurred up to September 1942, when the patient was lost from observation.

#### DIAGNOSIS

In addition to the usual history of contact dermatitis of the face and the appearance of the eruption, four outstanding characteristics were observed in all these cases. 1 The dermatitis is subacute. Vesiculopapules were mentioned by Fox,<sup>1</sup> but were not observed, even with a lens, in any of these patients. 2 The dermatitis tends to be bandlike with well defined borders, and there is a narrow band of normal skin between the borders of the dermatitis and the margins of the lid (5 cases). 3 When the dermatitis involves most of the cutaneous surface of the upper lids a narrow band of normal skin along the tarsal fold tends to divide the dermatitis into two bands (2 cases). Points 2 and 3 may be explained by the fact that the frame of the curler is applied at a slight angle, the handle being held away from the face so that the knife slides along the surface of the lid, and just above the lid of the margin it loses contact with the surface of the lid to clamp the eyelashes. The skin of the

<sup>1</sup> Curtis, G. H., and Netterton, E. W. Contact Dermatitis of the Eyelids Due to Rubber in an Eyelash Curler. Arch. Dermat. & Syph. 40: 847 (Dec) 1939.

upper lid is often pinched a few millimeters above the base of the eyelashes, and the skin of the lower lid is pinched a few millimeters below the margin. The tarsal fold escapes contact with the knife. The eyelashes of the upper lids are curved sharply upward, or there is almost an elbow bend of the distal part (all 7 cases). All patients had positive reactions to patch tests with the rubber fillers, and the dermatitis promptly healed after the patients stopped using the curlers.

These features distinguish the dermatosis from more common eruptions on the eyelids, such as seborrheic eczema, lichen chronicus simplex,

0.01 per cent in 90 per cent alcohol, diphenyl guanidine in crystals and in dilutions of 0.25 per cent, 0.1 per cent and 0.01 per cent in 90 per cent alcohol, new rubber fillers (*a*) obtained from the manufacturer of the instrument, rubber fillers (*b*) which were the same fillers soaked in 5 per cent sodium hydroxide one month and washed in running water for twenty-four hours, rubber fillers (*c*) supplied by the manufacturer and said to be "gyp" fillers, that is, fillers not put in the instruments by the manufacturer, ordinary rubber bands (*d*), and petrolatum and 90 per cent alcohol as controls. The patch tests

TABLE 1—Results of Patch Tests with Ingredients of Rubber Fillers

| Case | Rubber Fillers |     |     | Rubber Band (D) | 5% Sulfur | 5% Lead Oleate | Zinc Oxide Powder | Petrolatum, Control | Comment  |
|------|----------------|-----|-----|-----------------|-----------|----------------|-------------------|---------------------|--|
|      | (A)            | (B) | (C) |                 |           |                |                   |                     |  |
| 1    | +              | +   | 0   | 0               | 0         | 0              | 0                 | 0                   | Not available for detailed investigation                                   |
| 2    | +              | +   | —   | —               | —         | —              | —                 | —                   | Tests made 4 years later, delayed reaction (96 hr) vesicles seen with lens |
| 3    | —              | 0   | —   | —               | —         | —              | —                 | —                   | Tests made 2 years later   |
| 4    | +              | +   | ±   | —               | —         | —              | —                 | —                   | Tests made 1 year later  |
| 5    | —              | +   | —   | +               | —         | —              | —                 | —                   | Tests made 4 years later   |
| 6    | +              | +   | —   | ±               | —         | —              | —                 | —                   | Tests made 3 years later   |
| 7    | —              | +   | 0   | 0               | 0         | 0              | 0                 | 0                   | Not available for detailed investigation                                   |

+ = positive ± = doubtful, — = negative, 0 = not tested

TABLE 2—Results of Patch Tests with Ingredients of Rubber Fillers

| Case | Phenyl Beta Naphthylamine |    |      |       | Diphenyl Guanidine |       |      |       | Ethyl Alcohol (90%) Control | Comment   |
|------|---------------------------|----|------|-------|--------------------|-------|------|-------|-----------------------------|---|
|      | Crystals                  | 1% | 0.1% | 0.01% | Crystals           | 0.25% | 0.1% | 0.01% |                             |   |
| 1    | 0                         | 0  | 0    | 0     | 0                  | 0     | 0    | 0     | 0                           | Not available for study   |
| 2    | +                         | —  | ±    | —     | —                  | —     | —    | —     | —                           | Reaction to crystals of phenyl beta naphthylamine no stronger than to dilutions |
| 3    | +                         | —  | ±    | ±     | —                  | —     | —    | —     | —                           | Same as 2   |
| 4    | —                         | —  | +    | +     | —                  | —     | —    | —     | —                           | Crystals of phenyl beta naphthylamine caused vesiculation (mild)                |
| 5    | —                         | —  | ±    | —     | —                  | —     | —    | —     | —                           | Same as 2 and 3   |
| 6    | —                         | —  | ±    | —     | —                  | —     | —    | —     | —                           | Same as 2 and 3   |
| 7    | 0                         | 0  | 0    | 0     | 0                  | 0     | 0    | 0     | 0                           | Same as 1   |

+ = positive ± = doubtful — = negative, 0 = not tested

topic dermatitis, eczematous contact dermatitis due to other allergens, lupus erythematosus and nonspecific eczematoid eruptions.

#### CLINICAL INVESTIGATION

Dr. Louis Schwartz, Chief of the Dermatoses Investigations Section, United States Public Health Service, obtained a statement from the manufacturer that the rubber fillers consisted mainly of smoked sheet with small amounts of sulfur, lead oleate and zinc oxide. Diphenyl guanidine (0.25 per cent) was added as an accelerator and phenyl-beta-naphthylamine (1 per cent) as an antioxidant.

Five patients cooperated by having patch tests (see tables 1 and 2) with the following substances: latex, 5 per cent sulfur in petrolatum, 5 per cent lead oleate in petrolatum, zinc oxide powder, phenyl-beta-naphthylamine in crystals and in dilutions of 1 per cent, 0.1 per cent and

were applied for forty-eight hours, and the test sites were observed at the end of seventy-two hours, ninety-six hours and one week. A reaction was considered positive if it persisted longer than ninety-six hours and doubtful if it was a transient erythema, disappearing within seventy-two hours. The reactions are tabulated in tables 1 and 2 as positive, doubtful and negative. In case 4 there occurred the only reaction manifested by vesiculation (3 plus).

#### COMMENT

Phenyl-beta-naphthylamine and diphenyl guanidine were immediately suspected as the most probable causative allergens when the composition of the rubber fillers was known. Schwartz and Tulipan<sup>4</sup> mentioned these two

4 Schwartz, L., and Tulipan, L. A Textbook of Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, chap 4, p 44.

substances in rubber as causes of contact dermatitis among workers. They are also included in Weber's list of irritants.<sup>5</sup> Diphenyl guanidine ( $\text{NH C}_6\text{H}_5\text{NH}_2$ )<sub>2</sub> is a white crystalline powder<sup>6</sup> with a melting point of 147 to 148 C, 9.1 Gm is soluble in 100 Gm of 90 per cent alcohol at 20 C. It is only slightly soluble in cold water and slightly soluble in ether but is very soluble in hot alcohol or ether. The substance is used as an accelerator in the manufacture of rubber. Phenyl-beta-naphthylamine ( $\text{C}_{10}\text{H}_7\text{NH C}_6\text{H}_5$ ) is a white crystalline powder<sup>7</sup> soluble in alcohol or ether and very soluble in hot alcohol or ether. It is used as an antioxidant in the manufacture of rubber.

Phenyl-beta-naphthylamine was the causative allergen in the 5 cases in which patch tests were made (tables 1 and 2) and probably was the cause of the dermatitis in the 2 cases which were not available for detailed study. In case 5 there was definite hypersensitivity to an ordinary black rubber band and in case 6 a doubtful reaction to the rubber band. The 2 patients were also hypersensitive to the rubber of hose supporters. The causative allergen in the rubber of hose supporters and the shoe lastex (cases 5 and 6) probably was some chemical other than phenyl-beta-naphthylamine since 1 of the patients with a positive reaction to phenyl-beta-naphthylamine had a negative reaction to the rubber of the hose supporter clamp and lastex. It is also improbable that the chemical in the ordi-

nary rubber band to which these 2 patients reacted was phenyl-beta-naphthylamine, since the rest of the patients had negative reactions to the rubber band. These observations are in accordance with the specificity of cutaneous hypersensitivity.

I cannot explain the doubtful reaction, unless it is considered negative in case 4 to the "gyp" rubber filler as in the other cases there were no reactions. Patch tests were made on this patient on two occasions with two patch tests each at a different site, and all four tests elicited doubtful reactions.

The patch test results of which are recorded in tables 1 and 2 (except cases 1 and 6) were applied from one to four years after the original patch tests with the rubber fillers of the patients' curlers. This is additional confirmation of the fact that cutaneous hypersensitivity tends to be long lasting.

#### SUMMARY

Seven cases of contact dermatitis due to sensitivity to the rubber filler of eyelash curlers were observed. In 5 cases the allergen was found to be phenyl-beta-naphthylamine, an antioxidant used in the manufacture of rubber fillers. In addition to the history of contact and positive reactions to patch tests the dermatitis may be distinguished from other common dermatoses of the eyelids as well as from eczematous contact dermatitis due to other allergens by the facts that (1) the dermatitis is subacute rather than acute vesicular, (2) it tends to occur in linear bands, (3) if it involves the whole of the upper lid there is a narrow band of normal skin along the tarsal fold and between the dermatitis and the margin of the lid and (4) the eyelashes show artificial curling.

<sup>5</sup> Weber, L. F. External Causes of Dermatitis. List of Irritants, *Arch Dermat & Syph* **35** 129 (Jan) 1937.

<sup>6</sup> Eastman Kodak Company.

<sup>7</sup> E. H. Sargent & Co.

# SCROTAL TONGUE AND ITS INHERITANCE

NORMAN TOBIAS, M D

ST LOUIS

Scrotal tongue is also known as grooved, furrowed, wrinkled, fluted, plicated or ribbed tongue. According to Prinz and Greenbaum<sup>1</sup> scrotal tongue affects about one half per cent of the population.

The anomaly is usually familial or congenital. It involves the dorsum of the tongue, which may be lobulated or present convolutions or ridges similar to the topography of the scrotum. The ordinary markings of the surface of the tongue are exaggerated and the fungiform papillae are prominent. In some cases the grooves radiate from a central depression resembling the ribs of a leaf. The size and number of grooves, which are often symmetric, are variable.

Berggreen<sup>3</sup> found that it seemed to localize such diseases as lingua geographica, lichen planus and syphilis. It may be associated with other nevic conditions and is often found in acromegaly. Butlin and Spencer<sup>4</sup> suggested gout and syphilis as predisposing causes of the rare acquired or pseudoscrotal tongues.

Differential diagnosis is to be made from the "cobble-stone" tongue of late syphilis, lymphangioma and cerebriform nevus.

Treatment is of no avail, as the anomaly is permanent.

## REPORT OF CASES

CASE 1—Mrs L. R., aged 62, had had a scrotal tongue ever since she could remember. About five

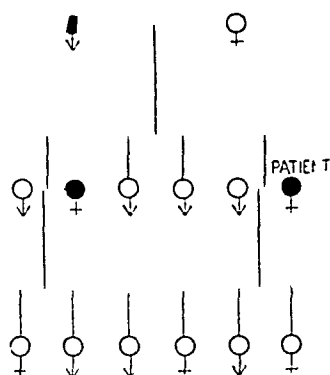


Chart 1—Pedigree of L. R., showing inheritance of scrotal tongue

The surface of the tongue may present a glazed appearance, and in about 25 per cent of the cases there is some evidence of macroglossia which may cause perleche.

According to Cockayne<sup>2</sup> the anomaly is inherited as an irregular dominant.

Symptoms are usually absent. Glossodynia is a rare complaint. In most cases scrotal tongue is found in the course of a physical examination.

Scrotal tongue may predispose to perleche, nonspecific glossitis and geographic tongue.

1 Prinz, H., and Greenbaum, S. S. *Diseases of the Mouth and Their Treatment*, Philadelphia, Lea & Febiger, 1935.

2 Cockayne, E. A. *Inherited Abnormalities of the Skin and Its Appendages*, London, Oxford University Press, 1933, p. 95.

3 Berggreen, P. Practical Importance of Scrotal Tongue, *Dermat. Wchnschr.* 102:421 (April) 1936.

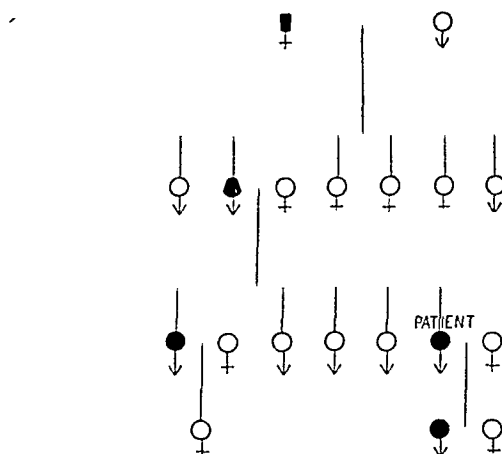


Chart 2—Pedigree of M. M., showing inheritance of scrotal tongue

years before consulting me for this disease a geographic tongue developed for which she consulted numerous physicians and consumed various amounts of vitamin products without results. For the last six months she had complained of glossodynia, and cancerophobia has developed. Her pedigree is illustrated in chart 1.

CASE 2—M. M., aged 55, a traveling salesman, presented himself for a localized neurodermatitis of the extensor surface of the left forearm. In the course of the examination the tongue was found to be of the scrotal type. Chart 2 illustrates the inheritance of the scrotal tongue.

## SUMMARY

Scrotal tongue is inherited as an irregular dominant. Two cases are described, in 1 of which geographic tongue was present.

634 North Grand

4 Butlin, H. T., and Spencer, W. G. *Diseases of the Tongue*, London, Cassell & Co., 1900.

# Clinical Notes

## AN IMPROVED METHOD FOR PREPARING PERMANENT SLIDES OF FUNGUS CULTURES

J WALTER WILSON, M D, LOS ANGELES

The method usually employed to preserve a specimen of a fungus colony which has been prepared for microscopic study is to "ring" the edge of the cover slip with balsam, petrolatum, de Khotinsky cement, melted shellac or some similar preparation. With this method it is difficult to prevent the formation of small cracks through which the fluid of the specimen evaporates in a few weeks or months. Also, the cover slip is not firmly attached to the slide, and gentle handling is necessary to avoid dislodging and destroying it. Such specimens usually become worthless after a short time, and students are handicapped unless fresh mounts are prepared each time they are desired.

By placing the specimen between a cover slip of the conventional size (22 mm) and a smaller one (15 mm or less, round or square) and mounting both as a unit in balsam, one can make preparations which, it is believed, will not deteriorate. The method, adapted from that of Diehl,<sup>1</sup> is as follows. The smaller cover slip is placed on a small piece of blotting paper or filter paper, and a very small drop of clearing medium (lactophenol or a similar mixture) is placed in the center, a small fragment of the culture is then gently mixed with the clearing medium, the large cover slip is dropped concentrically on this preparation and rather firmly pressed down. The paper will absorb any excess fluid, although it is preferable to avoid any such excess. The pressure should not be so great that air bubbles will form when it is released.

Two or three large drops of balsam or clarite are then placed in the center of a glass slide, and both cover slips (with the thin layer of the desired specimen which they contain) are lifted and without being turned over are dropped on the area covered with balsam. Gentle pressure may be maintained until the balsam has dried by allowing a small empty vial to rest on the cover slip. Any excess of balsam should be removed in order to allow the thin layer to become well hardened at its edges, but here also it is preferable to avoid any excess.

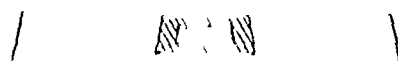
By this method a band which measures 3.5 mm in diameter and which surrounds the fluid layer entirely is completely filled with a thin layer of balsam the outer edges of which are as firmly hardened as in a properly prepared histopathologic section. The specimen may be examined under oil immersion if desired, since only a single thin cover slip intervenes between the objective and the specimen. The immersion oil

which has become popular in recent years—18 per cent alpha bromonaphthalene in light liquid petrolatum—is preferable to cedarwood oil because it is not sticky and does not dry, moreover, it may be rinsed off the cover slip with chloroform, carbon tetrachloride or ether without softening the balsam seal. Cedarwood oil requires xylene for its removal, which also softens and dissolves balsam, furthermore, as rinsing usually is insufficient, the substance must be wiped off and the cover slip is thereby frequently dislodged.

In addition, this method may serve other purposes. If small cover slips are routinely employed when one is making any of the ordinary microscopic examinations in saline solution, potassium hydroxide solution or solution of formaldehyde U S P, such specimens as are subsequently found interesting may be preserved for as long as the structures maintain their identity in such solutions simply by placing two or three drops of balsam on the small cover slip and dropping a large cover slip concentrically over it. Such preparations as



Method of Assembly



Completed Specimen

Method for preparing permanent slides of fungus cultures

these cannot, however, be viewed under oil immersion, as two thicknesses of cover slip and a layer of balsam intervene. If small cover slips are unobtainable, substitutes satisfactory for most purposes may be made by punching disks of about 1 cm in diameter from a sheet of cellulose acetate of from  $\frac{5}{1000}$  to  $\frac{1}{100}$  inch (0.127 to 0.254 mm) in thickness. Washed roentgenographic films may be used for this purpose, although they add a bluish shade. However, such plastics cannot be employed if potassium hydroxide is used, because they are softened and clouded by it.

It is hoped that this suggestion may result in more extensive collections of interesting and unusual material for study than are available at present.

2007 Wilshire Boulevard

From the Department of Dermatology of the University of Southern California

<sup>1</sup> Diehl, W. W. Improved Method for Staining Microscope Mounts. Science 69: 276, 1920



## Correspondence

### COURSE IN TROPICAL DERMATOLOGY

*To the Editor* —I returned last week from Mexico, D F, where I attended the course in tropical dermatology that was conducted by the Mexican Society of Dermatology, and I thought that it might interest the readers of the ARCHIVES to know that the course was so well planned and conducted that all the American dermatologists who attended were unanimous in their enthusiasm and praise for it. The course was conducted by the Mexican Society of Dermatology in cooperation with the Faculty of Medicine of the University of Mexico and the National Department of Public Health.

The subjects presented were pinta, onchocercosis, syphilis, leprosy, mycosis, leishmaniasis and lymphogranuloma venereum. An interesting introductory lecture on "Characteristics of Dermatology in Mexico" was delivered by Dr Jesus Urueña, the venerable and esteemed Doyen of Mexican dermatologists. The striking disease pinta was presented by Dr Gonzales Herrejon, who had devoted many years to intensive study of the subject and who, incidentally, was among the first students to suggest that pinta is a spirochetosis. Dr Manuel Baez, of the Tropical School of Medicine, discussed the subject of onchocercosis. In his lectures he not only gave a vivid picture of the disease but gave us also some insight into the great difficulties encountered by physicians who are concerned with public health in Mexico. He also told of the marvelous progress that is being made in public health work, for instance, blindness from onchocercosis has already been completely eradicated. The subject of leprosy was interestingly presented by Dr Fernando Latapi, who has long been an authority on that disease. He was convincing in his advocacy of the Brazilian classification of leprosy into lepromatous, tuberculoid and indeterminate types, presenting in support of his thesis a number of patients with each type of leprosy and the Lucio type of spotted leprosy, with which Latapi has worked so long. Dr Ignacio Gonzalez Guzman, Director of the Faculty of Medicine of the University of Mexico, collaborated with an inspiring lecture on the histopathology of leprosy. Dr Julio Bejarana, the syphilologist, in his presentation of the subject of syphilis, stressed only those features of the disease that are unique to Mexico and Spain, where he has had a large experience with syphilis. He presented several cases of a type of impetiginous secondary stage eruption, which is seen commonly in Mexico but which was unfamiliar to Americans. Dr Antonio Gonzales Ochoa in his presentation of the mycoses limited himself to mycetoma, sporotrichosis, chromomycosis and tinea imbricata. Dr Latapi discussed his experiences with thallium acetate in the treatment of tinea capitis. Leishmaniasis was discussed by Dr Gutierrez, Prof Beltran discussed the laboratory diagnosis of leishmaniasis. Dr Oswaldo Arias, who treated the subject of lymphogranuloma venereum, demonstrated his points with the presentation of a number of patients with the anorectal syndrome, in whom striking clinical improvement was obtained by a special preparation of sulfathiazole injected directly into the lesions.

All the subjects were presented in the form of lectures, clinical presentations, laboratory demonstrations and round table discussions. The clinical material was carefully chosen and uniformly excellent. The lectures and round table discussions were stimulating, so that in all the course was both interesting and instructive. There were supplementary lectures by specialists in related fields, such as ophthalmology, parasitology, histopathology and laboratory technology. There was an unusually interesting motion picture of pinta. In addition, we were taken to visit the National Leprosarium, also the village of Iguala (which is "the home of pinta") and several new beautiful and well equipped public hospitals. The Mexican Society of Dermatology and the Mexico National Academy of Medicine both held special meetings to which we were invited.

Captain Orlando Canizares, Army of the United States, acted in a liaison capacity and as interpreter for the lecturers who spoke Spanish. He contributed greatly to the success of the course. Altogether it was a pleasant experience, for, in addition to the course, Mexico is an ideal place for a vacation and our hosts were most gracious and hospitable to us and our families. Our contacts throughout were characterized by an unusual friendliness and informality that added immeasurably to the pleasure of the trip. Unfortunately, because of travel limitations in this country, only nineteen American physicians were able to be present. It is hoped that the course will be offered again when wartime restrictions on travel are removed, so that others from this country may be privileged to attend it. Those of us who were there are grateful to both Dr Howard Fox and Dr Leon Goldman, for we understand that it was at their suggestion that the course was given.

HENRY RATTNER, M D, Chicago

104 South Michigan Avenue

### IMPETIGO BULLOSA IN THE TROPICS

*To the Editor* —Captain Charles S. D'Avanzo's article, "Impetigo Bullosa in the Tropics," which appeared in the July 1945 issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (52:28, 1945) was read with great interest, since in the past two months I have seen and treated over 100 patients with impetigo bullosa in a station hospital located in the central part of Louisiana.

Captain D'Avanzo's description of the lesions is perfect. The interesting finding of the definite demarcation between the clear fluid in the upper part and the heavier yellow fluid in the dependent part of the bullae has been an almost constant finding among my patients also. The lesions are usually located in the axillas and groins, however, several patients with a severe form of the disease presented generalized bullous lesions.

I have found a satisfactory form of treatment. The bullous lesions are opened, and drained, and the tops are removed with observance of sterile precautions. The crusted lesions are soaked with 1:9,000 potassium permanganate solution, and the crusts are removed. Then penicillin cream is rubbed into all lesions.

In preparing penicillin cream I use 500 units of penicillin to 1 Gm of a water-soluble emulsion base (emulsion base I [medium], Pillsbury, D M, Sulzberger,

M B, and Livingood, C S Manual of Dermatology, Philadelphia, W B Saunders Company, 1942, p 379), which does not seal up the secretions to cause maceration and spread of lesions In the treatment of severe and generalized forms 20,000 units of penicillin is given intramuscularly every three hours in conjunction with the local treatment

I do not use sulfonamide compounds since the aforementioned method of treatment works admirably and all my patients have been cured in from four to eight days Furthermore, there is always the possibility of producing sulfonamide sensitivity from local absorption

SIMON S RUBIN, M D, Chicago  
4333 North Troy Street (18)

## News and Comment

### GENERAL NEWS

#### Courses in Mycology and Radiologic Physics —

The following courses will be available at the College of Physicians and Surgeons, New York

Medical Mycology (Dermatology 101-T), by Prof Rhoda W Benham, will be given for three hours on

Tuesday and Thursday mornings, with an additional lecture hour each week to be arranged The course will be given for thirteen weeks beginning Jan 3, 1946 The fee is \$25 for the course and \$5 for registration

Radiologic Physics (Ce-1), by Prof Edith H Quimby, consists of sixteen one-hour lectures, on Wednesdays at 7 30 p m, beginning Jan 9, 1946 The fee is \$50

Further information may be obtained from the Dean of the College of Physicians and Surgeons, 630 West One Hundred and Sixty-Eighth Street, New York

**American Board of Dermatology and Syphilology, Inc**—The next oral examination of the American Board for both group A and group B candidates will be held on June 6, 7 and 8, 1946 The written examination for group B candidates will be held on April 22, 1946 The closing date for the applications for both group A and group B candidates is March 1, 1946 George M Lewis, M D, 66 East Sixty-Sixth Street, New York, is the secretary

### DEATHS

Dr Kendal P Frost died in Los Angeles on Sept 27, 1945

## Obituaries

HENRY J F WALLHAUSER, M D

1865-1945

Dr Wallhauser was born in New York city in 1865. At the age of 5 years he moved to Newark, N J, where he later practiced for fifty-four years, the past forty as a dermatologist. He

His early dermatologic training was received under Prof George Henry Fox, of New York city. For forty years he was medical director and chief of dermatology and syphilology at the Newark



HENRY J F WALLHAUSER, M D

1865-1945

received the degree of M D at Bellevue Hospital Medical College, New York, in 1888. He died May 5, 1945, at the Hospital of St Barnabas and for Women and Children, Newark, N J.

Dr Wallhauser was a singer of note, and in his early days debated whether to become a professional singer or to study medicine.

City Dispensary. He administered the first injection of prophenamine salvarsan in New Jersey.

He was an enthusiastic gardener and won many prizes in flower competitions. He was also an ardent angler and had fished in many waters in this country and in Canada.

Dr Wallhauser's outstanding characteristic was his kindness to and consideration for every one. He was especially interested in young physicians and was a constant source of help and encouragement to them over a long period.

Dr Wallhauser was a fellow of the American Academy of Dermatology and Syphilology, the New York Academy of Medicine and the Academy of Medicine of Northern New Jersey. He was a specialist certified by the American Board of Dermatology and Syphilology, Inc., past president of the Essex County (N J) Medical Society, past president of the New Jersey Dermatological Society, member of the Manhattan Dermatologic Society, and consulting dermatolo-

gist to Mountainside Hospital, Montclair, N J, Overlook Hospital, Summit, N J, Essex County Hospital for Contagious Diseases, Belleville, N J, St Mary's Hospital, Orange, N J, and Newark Memorial Hospital, Newark City Hospital and Hospital of St Barnabas and for Women and Children, Newark, N J.

Dr Wallhauser's first wife, the former Rachel A Vogt, of Newark, died in 1937, leaving two sons, George M, of Maplewood, N J, and Dr H Andrew of Brooklyn. In September 1939 he married Vanneta Shaw Foist, of Mount Bethel Pa, who survives him, as do the sons. There are four grandchildren.

FRANCIS J McCAULEY, M D

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

ECTODERMAL DYSPLASIA WITH PARTIAL ANODONTIA  
M MICHAEL COHEN and RICHARD WAGNER, Am  
J Dis Child **68** 333 (Nov) 1944

This is a short report of a case of an incomplete type of hereditary ectodermal dysplasia. The singular features were the partial anodontia and the dystrophic changes in the nails of the fingers and toes. Microscopic examination of the skin revealed the presence of sweat glands.

GENERALIZED CUTANEOUS MONILIAL INFECTION ALBERT  
STRICKLER, Am J Dis Child **68** 382 (Dec) 1944

In a short article Strickler reviews the previous reports on generalized cutaneous moniliasis. He briefly reports a case of the disease in a 2 year old child. There was involvement of the scalp, simulating a pyoderma. On the forehead, arms, hands and thighs there were uniform circinate lesions with clear or slightly scaly centers and crusted elevated scaly borders. The finger and toe nails presented a loss of transparency, a dark yellowish brown color, thickening and fragility. A mild degree of paronychia was present. The general health was unaffected. Therapy with 50 per cent alcohol and an ointment containing iodine proved beneficial.

HAIR LACQUER DERMATITIS IN INFANTS FROM CONTACT  
WITH MOTHER'S HAIR MILTON PLOTZ, Am J Dis  
Child **68** 409 (Dec) 1944

This is an interesting report of 2 cases of hair lacquer dermatitis in infants due to contact with the mother's hair. In the first case a dermatitis was present on the inner aspects of both forearms, the right side of the neck, both cheeks and part of the forehead.

In the second case a crusty erythematous dermatitis was present on the forearms, one cheek, most of the forehead and temple and the back of the neck.

Positive reactions were elicited in both cases to patch tests to the mother's hair lacquer. In both cases the eruption promptly disappeared when the mother discontinued the use of the lacquer.

NELSON PAUL ANDERSON, Los Angeles

SYPHILIS TRANSMITTED FROM A CONGENITALLY SYPH-  
ILITIC CHILD TO HIS OWN FATHER HOLLISS IN-  
GRAHAM and ALFRED HESSE, Am J Syph, Gonorr  
& Ven Dis **28** 733 (Nov) 1944

The authors report the transmission of syphilis from a mother to her child in utero and from the child after birth to the father, by contamination of his conjunctiva. White petrolatum which was applied to the child's nose for treatment of a syphilitic rhinitis was also applied from the same container by the father about his own nose, therefore it seemed to be the likely source of the father's infection.

REUTER, Milwaukee

HEREDITARY ECTODERMAL DYSPLASIA FRANCIS E  
BRUNO and HUGO T ENGLEHARDT, Ann Int Med  
**20** 140 (Jan) 1944

Bruno and Englehardt report the case histories of 3 siblings with sparse hair of a fine texture and with

nails of the fingers and toes which were short, thin and brittle and possessed a central concavity. In 2 of the cases the upper third molars were missing. The cases were regarded as examples of hereditary ectodermal dysplasia.

GUTTMAN, Philadelphia  
[ARCH NEUROL & PSYCHIAT]

TREATMENT OF HUMAN ANTHRAX WITH PENICILLIN  
FRANKLIN D MURPHY, ALFRED C LABOCCETTA and  
JOHN S LOCKWOOD, J A M A **126** 948 (Dec 9)  
1944

Three patients with uncomplicated cutaneous human anthrax without bacteremia were treated with penicillin. Prompt clinical response to penicillin was observed in all patients.

HENSCHEL, Denver

CEREBROVASCULAR ACCIDENTS FOLLOWING EPINEPHRINE  
INJECTIONS I L APPIEBAUM, J Allergy **15** 392  
(Nov) 1944

The author reports 2 cases of cerebrovascular accidents following the subcutaneous injection of 0.5 cc of epinephrine hydrochloride (1:1,000 solution).

Signs and symptoms of reaction included headache, palpitation, apprehension, slurred speech and hemiplegia. Complete recovery occurred in 1 patient within two hours, but the hemiplegia and facial palsy persisted in the other patient for five weeks.

URTICARIA CAUSED BY CHLORINATED DRINKING WATER  
M J GUTTMAN, J Allergy **15** 395 (Nov) 1944

The author reports 2 cases of urticaria and angio-neurotic edema in which chlorinated drinking water was found to be the cause of the symptoms.

Cutaneous tests with table salt elicited positive reactions in both patients.

MINDELSOHN, New York

TREATMENT OF EXTERNAL OTITIS I LOCAL SULFON-  
AMIDE THERAPY BEN H SENTURIA, Laryngoscope  
**54** 277 (June) 1944

External otitis is an important disease in the warmer climates. The causative organisms are probably a mixture of both bacteria and fungi. The bacteria may be various kinds of streptococci, staphylococci, diphtheroids and Bacillus pyocyaneus. The fungi may be spores of Penicillium, Aspergillus and Monilia. They are saprophytic fungi. True pathogenic fungi are rarely found.

Fungi need carbohydrates for their growth. They flourish in ear wax. Moisture is necessary for them to obtain close contact with their source of energy. Toxins are produced by the growth of the fungi. These irritate the surface epithelium. The bacteria present then invade this irritated epithelium.

Signs and symptoms vary from a feeling of blockage, dryness, itching, scaling or slight tenderness on manipulation of the external canal to varying amounts of pain, edema of the wall of the canal, glandular swelling and slight fever.

In treatment, a mixture of sulfanilamide, sulfathiazole and zinc peroxide powders (4:2:2) was found most efficacious. It was blown into the ear after this had

been cleaned mechanically and with hydrogen peroxide

The patients were seen daily for several days. Sedation was given as necessary. As the condition improved, irrigation with sodium bicarbonate solution was used to wash out all the accumulated debris and powder. Irrigation was done only when the edema and the tenderness had subsided enough to permit drying of the canal afterward. This was followed with instillation of alcohol. In several minutes this was allowed to run out. The residuum in the canal soon evaporated. Powder was then reapplied and left in for a week. The patient was cautioned against getting water into or about the ears, and swimming was forbidden.

In all patients with acute infection the disease responded well, only 1 patient in 33 requiring more than seven days for a complete cure. No recurrences were observed. In other patients, as a control, treatment consisted of dry wipes and the use of alcohol and of sulfanilamide in alcohol. In these the disease did not respond so quickly and some recurrences were noted. Auditory acuity was unaffected.

HITSCHLER, Philadelphia [ARCH OTOLARYNG]

DERMATOLOGIC THERAPY IN THE TROPICS THEODORF M COHEN, U S Nav M Bull 42 1119 May) 1944

The poor results encountered in dermatologic therapy in the tropics are due frequently to an intolerance to drugs which can be used in a temperate climate with impunity.

An analysis of cases revealed the following groups: fungous infections, 36.6 per cent, dermatitis venenata, 9.9 per cent, pyodermas, 9.9 per cent, and miscellaneous dermatologic entities, 43.6 per cent. Except for yaws and leprosy, the groups included the dermatoses usually found in the United States.

Phenol, mercury and sulfur, employed in various vehicles, even though diluted, produced irritation of the skin. This effect was due to the increased hyperhidrosis and dampness of the skin caused by the high humidity.

Twenty-four per cent of the pyodermas were the tropical ulcers, which were usually preceded by a traumatic lesion, coral cuts or insect bites. These were treated with (1) complete rest in bed and elevation of the leg, (2) potassium permanganate, diluted 1:15,000 and applied in a compress for twenty minutes three times a day, and (3) 5 per cent sulfathiazole triethanolamine 10 per cent in a water in oil emulsion base.

All acute dermatoses, regardless of the cause, were treated with wet dressings until all signs of acute inflammation had subsided. All crusts and dead skin were removed before ointment or other topical applications were employed. Overtreatment was found to be the most frequent cause of chronic dermatitis.

ROBIN, South Bend, Ind

THE PHENOL-CAMPHOR TREATMENT OF DERMATOPHYTOSIS BENTLEY PHILLIPS, Brit J Dermat 56:219 (Nov-Dec) 1944

composed of 137 cases of tinea pedis, 83 cases of tinea cruris and 10 cases of tinea axillaris. In all cases the medicament used was a mixture of equal parts of phenol and camphor, with the following results: The average time for cure of tinea cruris was four and three-tenths days, tinea pedis four and a half days and tinea axillaris four and nine-tenths days. There were no failures of treatment in 230 patients treated with phenol and camphor. In only 17 per cent of the cases was there a relapse during three months' follow-up. No toxic reactions, either local or general, were observed. The mixture of phenol and camphor is considered by the author to be an innocuous medicament and a specific remedy for these forms of dermatophytosis.

ANGIOKERATOMA E LIPMAN COHEN, Brit J Dermat 56 228 (Nov-Dec) 1944

The author reports a case of angiokeratoma (Mibelli) in a girl aged 16. For four years she had spots on her right leg. Two years after the onset she had roentgen ray treatments of the lesions, and they became gray and harder but were unchanged in size. On examination, the lower two thirds of both legs were reddish purple, and they felt cold to the touch. On the back of the right leg over the proximal end of the achilles tendon was a group of warty swellings, the biggest being  $\frac{3}{4}$  inch (1.9 cm) in diameter. Distal to the warty swellings and also on the calf were a few lentil-sized circumscribed (0.03 Gm) discrete reddish purple macules. Treatment consisted of ingestion of  $\frac{1}{2}$  gram of thyroid daily and the application of solid carbon dioxide to the warty lesions. Improvement was steady, and the growths became gradually smaller, their warty tops eventually falling off.

According to the author, a search of the literature has failed to reveal any previous example of such lesions occurring on the back of the leg. In all previous cases of the disease the fingers, hands, toes or scrotum have been the sites of involvement.

BLUFARB, Chicago

AMEBIC INFECTION OF THE VULVA COMPLICATING GRANULOMA PUDENDI J B CLELAND, J Trop Med & Hyg 47 54 (Oct-Nov) 1944

The author reports the case of a 22 year old Australian aboriginal woman who was admitted to the hospital for an extensive granulomatous ulceration of the pudenda, of three weeks' duration. The Wassermann and Mantoux reactions were negative, and no spirochetes were found on dark field examination. Leishmania bodies were found on direct smears. Despite intravenous injections of antimony and potassium tartrates, she died within three weeks.

A biopsy of the vulva was performed shortly after death, and there were pockets of endamebas in the tissues extracellularly.

The author stated the belief that the amebic infection of the granulomatous area was secondary to amebic dysentery, though thirty-six hours after death no amebas could be found in the intestinal walls. A similar case in a man had been observed by the author a few years previously.

LAYMON, Minneapolis

IMPETIGO CONTAGIOSA TREATED WITH MICROCRYSTALLINE SULFATHIAZOLE JOSEPH W BIGGER and GEOFFREY A HODGSON, Lancet 2 78 (July 15) 1944

Of 50 patients with impetigo contagiosa who were treated with microcrystalline sulfathiazole, 48 were cured in an average of five and three-tenths days. Ooz-

ing usually ceased within one or two days, and the epithelium rapidly regenerated. The cure was sometimes delayed by the appearance of fresh lesions. The time required for the cure of the disease was shorter than with any treatment previously used. In only 1 patient treated with microcrystalline sulfathiazole did sensitivity develop.

LANGMANN, New York  
[AM J DIS CHILD]

DISCUSSION OF SOME POINTS RELATED TO LYMPHO-  
GRANULOMA VENEREUM JOSE MAY, Rev med de  
Rosario 32 3 (June) 1942

May prefers the term paradenolymphitis to lymphogranuloma. He lists the following signs as important in the early diagnosis of lymphogranuloma venereum: (1) early regional edema, (2) lymphangitis of the genitals (in men), (3) positive Frei reactions, particularly in cases of infection which are not observed clinically, and (4) the ocular syndrome—(a) kinky and thickened vessels above the papilla, (b) hyperemia of the papilla and retina, (c) blurring of the disks, (d) dilated retinal veins, (e) choked disks, (f) diastolic

hypertension of the retinal artery, (g) hypotension of the eye [less than 15 mm of mercury in 80 per cent of the cases], (h) visualization of the nerves in the cornea and (i) increased cells and protein content in the spinal fluid.

The ocular syndrome can be observed in cases of acute as well as of chronic lymphogranuloma. May also observed that 50 per cent of the patients with tabes dorsalis had a positive reaction to the Frei test and that the same test frequently elicited positive reactions in patients with epilepsy, thromboangitis obliterans, induratio penis plastica (81 per cent had positive Frei reactions) and Dupuytren's contracture (93 per cent of 16 patients showed the ocular syndrome characteristic of lymphogranuloma venereum). May suggests that it would be interesting to consider the virus of lymphogranuloma venereum as a possible causative agent in some cases of the aforementioned diseases.

Sulfonamide compounds, antimony and potassium tartrate, copper, Frei antigen, and strong solution of iodine U S P are mentioned as therapeutic agents for lymphogranuloma venereum.

LAYMON, Minneapolis



# Society Transactions

## LOS ANGELES DERMATOLOGICAL SOCIETY

WILLIAM H. GÖCKERMAN, M.D., *Chairman*

CLEMENT E. COUNTER, M.D., *Secretary*

May 6, 1944

### A Case for Diagnosis (Fixed Bismuth Dermatitis?) Presented by DR. HAL E. FREEMAN

The patient is a Negro woman, aged 31. Two years ago she was found to have syphilis of the central nervous system. Until three months ago she had received nine injections of oxophenarsine hydrochloride, twenty-nine injections of tryparsamide and nineteen injections of a bismuth preparation. Beginning three months ago six more injections of bismuth subsalicylate, in doses of 1 cc., were given. The present eruption began two weeks after the first injection of the last series. The first lesion of the present eruption was an oval plaque, about 3 cm. long, on the left thigh. Soon another, similar, lesion appeared on the abdomen. In the last ten days numerous other lesions have developed.

The patient is a moderately well nourished Negro woman. On the anterior surface of the left thigh and on the lower abdominal wall are raised, bluish red, exuding and secondarily excoriated plaques, approximately 6 by 7 cm. Erythematous papules and vesicles and pustules are present on the arms, chest and face. These are about 3 mm. in diameter. There is a redness of the right side of the soft palate. There is no evidence of cardiovascular syphilis.

The urine and blood cells were normal. The Kolmer reaction of the blood was 1 plus and the Kline reaction 3 plus in examinations made two months ago. Examinations of the cerebrospinal fluid performed eighteen months ago revealed 70 cells, a Kolmer curve of 44400, and a colloidal mastic curve of 2221100000.

#### DISCUSSION

DR. M. E. OBERMAYER: This dermatosis is a lichenoid toxic dermatitis, probably from heavy metals. Bismuth may cause such an eruption. The fact that Koebner's phenomenon was present in a linear scratch mark and that the patient gave a history of having had lesions on the oral mucosa makes me think that the dermatosis is vesicular lichen planus.

DR. M. T. R. MAYNARD, San Jose, Calif.: I agree with the diagnosis. This case reminds me of a case presented at the last meeting of the American Academy of Dermatology. The patient had a lichenoid dermatitis, and the histologic study revealed a lichen planus picture.

DR. KENDAL FROST: I have a patient in whom typical lichen planus developed while he was taking neoarsphenamine. This eruption cleared after a course of arsenicals and returned with a later course. The histologic picture, as well as the clinical picture, was one of lichen planus.

DR. L. F. X. WILHEIM: I have a patient at present who has a generalized lichen planus type of eruption, the onset of which occurred during a course of injections of an arsenical and which is continuing while she is receiving bismuth therapy.

DR. W. H. GÖCKERMAN: I think that all dermatologists have seen these cutaneous pictures definitely produced by the arsenicals and probably also produced by bismuth. One might speculate as to whether toxins of various types are capable of producing what is called lichen planus. It is likely that so-called lichen planus is only a morphologic picture, which has a variety of causative factors, hence its varied responses to treatment. It is interesting to me to see the very drugs that are of value in the clearing of lesions of lichen planus produce an appearance of lichen planus. It is true that the classic picture of lichen planus is only occasionally produced by these drugs, but at times it is impossible to say whether the eruption is due to the drugs or to some unknown cause.

DR. HAL FREEMAN: The question I should like to hear discussed is whether it is safe to continue use of tryparsamide for this patient. Is the eruption due to bismuth or due to arsenic?

DR. CHRIS HALLORAN: About ten years ago Dr. Irving Bancroft and I studied a series of cases of this type. We found that it was the opinion of the French dermatologists that treatment should be continued despite the eruption. We observed 1 patient eight years later, and he still showed some of the pigmented spots. When some of these lesions were examined microscopically, they presented the picture of lichen planus. In three fourths of the cases studied then the eruption developed while the patient was being treated with arsenicals. Bismuth was the apparent cause of the eruption in only about one fourth of the cases.

DR. M. F. ENGMAN JR., St. Louis: To me lichen planus is a distinct clinical entity. There is nothing else exactly like it, but at times other diseases may bear a superficial resemblance. In this patient I could find no unmistakable lichen planus lesions. One does not think it uncommon in patients with syphilis under treatment with heavy metals to see an exacerbation of psoriasis or lichen planus. This may not be a contraindication for further treatment with heavy metals, but one must modify treatment to suit the particular case. In this patient the evidence points to bismuth as the cause of the eruption. It is still possible that the dermatitis was caused by something else. I should not consider this a definite contraindication for further antisyphilitic treatment, but further treatment must be undertaken with caution.

### Acute Monocytic Leukemia Cutis (Naegely Variety) Presented by DR. HAL E. FREEMAN

A woman aged 59 had severe rheumatic fever thirty-eight years ago. A generalized erythematous eruption began ten weeks ago. Pruritus, exfoliation and chilliness developed. Various-sized superficial and deeper cutaneous nodules and subcutaneous tumors have been present during the last three weeks.

The patient is well nourished but acutely ill. She has a generalized erythematous dermatosis. Many areas are excoriated. There are tumors at widely scattered locations, especially on the right buttock. These vary in size from 1 to 3 cm. in diameter. The face is edematous, presenting a leonine appearance. There is more edema in the periorbital area. On the chest, in the axillas, on the arms and on the left fore-

arm are numerous closely set papulovesicles, with a superficial dark crust and umbilicated like Kaposi's varicelliform eruption. These lesions appear to be superimposed on an indurated and edematous cutaneous background. There is inguinal lymphadenopathy. The spleen and liver are enlarged. There is cardiac insufficiency with decompensation evidenced by dyspnea. The temperature has varied between 99 and 104 F. The higher temperatures have been in the evening.

The urine showed a trace of albumin. The hemogram showed 12.5 Gm of hemoglobin per hundred cubic centimeters of blood. The color index was 0.9. There were 4,050,000 erythrocytes and 76,150 leukocytes, with 12 per cent polymorphonuclear leukocytes, 8 per cent lymphocytes, 1 per cent eosinophils and 2 per cent basophils. Eighty per cent of the monocytes were mature, 15 per cent were promonocytes and 5 per cent were monoblasts. Goodpasture's stain showed peroxidase granules present in monocytes.

Biopsy of a cutaneous tumor in the left groin revealed thinning of the stratum corneum, slight parakeratosis and a dense cellular infiltrate in the papillary portion of the corium. In localized areas throughout the corium and deeper fat were these infiltrating cells. They were monocytic or "transitional" in type. In places they had destroyed the prickle cell layers as well.

Six treatments with roentgen rays have been given in three weeks, each treatment consisting of approximately 75 r.

#### DISCUSSION

DR NELSON PAUL ANDERSON: I should like to congratulate Dr. Freeman on making the diagnosis in this case. I think that the eruption seen in this case is an excellent example of those occasionally seen in cases of the lymphoblastoma group. I do not believe, however, that this eruption is typical of monocytic leukemia. The only eruption typical of the monocytic type of leukemia is that characterized by small pea-sized plum-colored multiple cutaneous and subcutaneous nodules scattered over the body. In this particular case Dr. Freeman tells me that the peculiar glazed small impetiginous and pustular eruption on the breasts is of only two or three days' duration. The outlook of course in such cases is bad. I do not believe that such patients live long.

DR HAL E. FREEMAN: Radioactive phosphorus is desirable in any cases of lymphoblastoma, but so far none has been used in this case.

DR M. T. R. MAYNARD, San Jose, Calif.: At the University of California the use of radioactive phosphorus is considered limited.

DR P. K. ALLEN, San Diego, Calif.: I have had experience with a similar case, that of a young woman with granulomatous lesions of the vulva, groins and gums. The lesions had been present for three or four years without spreading to other areas. She was presented before the Los Angeles Dermatological Society two years ago, with granuloma inguinale. Biopsy in San Diego showed lymphosarcoma. The patient subsequently went to the Mayo Clinic, where biopsy sections were also pronounced to show lymphosarcoma, though the physicians were unable to arrive at a positive diagnosis. She received irradiated phosphorus with good results, though temporary. She was subsequently treated successfully with irradiated phosphorus in San Francisco and a third time, in San Diego, with only temporary cure. Subsequently the disease responded to massive vitamin therapy, mainly the B complex group. At the present time she is well.

CAPT ERVIN EPSTEIN (MC A US): I have treated a number of patients with radioactive strontium and phosphorus. This group included 9 or 10 patients with psoriasis and 1 with hemorrhagic sarcoma of Kaposi. The results were discouraging in this group. Sufficient radioactive strontium was administered to the patient with sarcoma to lower the hemoglobin to 40 per cent. In spite of this the lesions failed to respond, although they later cleared completely with conventional radiotherapy. Neither radioactive strontium nor phosphorus are deposited in the skin in sufficient amounts to be of therapeutic value. This was confirmed by the actual measurement of the amount of radiation in the tissues of these patients. Until some element, such as radioactive sulfur or arsenic, which is deposited primarily in the skin is produced in sufficient amounts, I doubt that radioactive chemicals will prove advantageous in the treatment of cutaneous diseases.

DR H. P. JACOBSON: Regarding the selective deposition of radioactive phosphorus in cutaneous tissues, I recall the case of a patient at the Los Angeles County Hospital Malignancy Service who presented extensive radiation necrosis of both buttocks, probably having resulted from radioactive phosphorus administered about one and a half years previously. It may be of interest in connection with the discussion regarding the management of this case to recall a limited experience with 1 case of chronic myelogenous leukemia. The patient was a middle-aged woman with a familial history of tuberculosis in members of two generations. She came to the malignancy board because of a large spleen reaching to the brim of the pelvis, 350,000 leukocytes and a terminal clinical picture of chronic myelogenous leukemia. Because of the hopeless outlook and on the assumption that sulfanilamide would depress the functioning of the bone marrow, I was given authorization by the tumor board to give this patient sulfanilamide. In a period of five weeks the spleen became smaller, so that it could not be palpated, and the leukocyte count was down to 9,000. A remission had been obtained. A secondary anemia, which the patient had had prior to and during the sulfonamide therapy, was treated by a transfusion, which resulted in one of those rare transfusion deaths. At autopsy specimens of all the blood-forming organs were obtained, and microscopic examination of tissue sections confirmed the observation that there was a remission of the leukemic process. My reason for failing to report the case at the time was conservatism and unwillingness to infer conclusions on the basis of 1 case. In citing this case I wish to suggest that in view of the apparent serious clinical problem presented by this patient, sulfanilamide therapy under close supervision might possibly offer some promise.

DR HAL E. FREEMAN: I appreciate Dr. Jacobson's suggestion, but I hesitate to give a drug which can as easily cause a leukocytosis as it can a leukopenia. Sulfonamide compounds have been used for various lymphoblastomas and, as far as I know, with no benefit. I think that from the practical point of view it might be interesting to mention that I saw this patient with these tumors and performed a biopsy. In the meantime a blood smear showed 90 per cent lymphocytes. A patient could not have a leukocyte count of 70,000 with 90 per cent lymphocytes without having splenic enlargement and considerable lymphadenopathy. This made me question the laboratory report, and I then had a Goodpasture peroxidase stain made; these unusual cells were found to be peroxidase positive, which rules out lymphocytes. This signifies, then, the Naegeli type of monocytic leukemia as opposed to the Schilling variety.

### Nodular Interstitial Glossitis Due to Syphilis

Presented by DR HARRY P JACOBSON

The patient, a woman aged 50, has a living daughter, who is well. She states that she never had a miscarriage. She is in good health.

About twelve years ago a "sore" developed on the left lateral aspect of the tongue. This lesion lasted several months and finally healed. Some time afterward other lesions developed on the tongue, to which she attached little importance, and she did nothing about them. Three years ago she consulted a physician, who made "saliva and blood tests" and told her not to worry. Three months ago the tongue was so painful that she consulted a "specialist." The latter first performed a biopsy and then treated her with topical applications as well as tablets of a sulfonamide drug internally for two months. When examined one month ago, she presented an irregular nodular infiltration of the anterior portion of the tongue, extending from the junction of the anterior and middle thirds on the right side in a diagonal line toward the left side of the tip. A deep necrotic linear fissure, about 2 cm long, is present on the dorsal surface.

Serologic tests of the blood serum elicited reactions as follows: Eagle flocculation test positive, Kline test, 4 plus, Hinton test, positive and Wassermann test, positive 4/44. The microscopic examination of the tissue removed for biopsy showed the surface covered with essentially normal stratified squamous epithelium, the basement membrane of which was everywhere intact. In the subepithelial connective tissue there was abundant inflammatory cellular infiltrate consisting chiefly of plasma cells, lymphocytes and other mononuclear cells. Near one end of the section the cellular exudate was denser and fairly well circumscribed. There was a small area of necrosis on the lateral surface. Interspersed among the inflammatory cellular elements were groups of fibroblasts, with spindle-shaped or ovoid nuclei. Near the opposite lateral surface a small fairly well circumscribed inflammatory focus was found, presenting a granulomatous appearance. Here and there were, in addition, some epithelioid cells and occasional multinucleated giant cells. Included in the section were some scattered bundles of striated muscle. These were infiltrated with the inflammatory cellular elements previously described. The composite histologic picture was that of a granulomatous type of inflammatory process. There was no evidence of a malignant tumor.

#### DISCUSSION

DR L F X WILHELM: I think that the possibility of an underlying malignant neoplasm must not be lost track of in a case like this. When I was practicing in New York, a physician in general practice brought in a patient with a lesion of the tongue who had a positive Wassermann reaction. He insisted on treating the patient for syphilis for six weeks. During that time the lesion became much larger, and the man died during the operation for total removal of the tongue.

DR H P JACOBSON: There is little to add to the presentation already made. The clinical features in the case are suggestive of (1) syphilis, (2) carcinoma and (3) actinomycosis. The serologic reaction of the blood is strongly positive (both complement fixation and precipitation). An adequate biopsy showed no evidence of malignant changes, but the architecture of the tissue was strongly suggestive of syphilis. I am fairly certain that the patient will respond to antisyphilitic therapy.

### Generalized Moniliasis and Trichophytosis

Presented by DR SAMUEL AYRES JR

B D R, a boy aged 6 years, has had pneumonia several times. He has also had gastroenteritis and pertussis and is underdeveloped. The present eruption began three years ago. His mother states that the eruption began on his chin after a mosquito bite. It has persisted there ever since, although improvement followed the use of sulfur soap. The lesions of the scalp and nails have never cleared. The eruption has been worse again during the past month. The child is below par physically and is considerably undersize and underweight. On the scalp are ill defined dry erythematous yellowish white scaling and crusted lesions. The hair is thinned. Erythematous scaly plaques are present on the ears and forehead. On the cheeks and across the nose the lesions assume a butterfly arrangement. Margins of lesions tend to have an ovoid circinate pattern, with peripheral activity. There are large yellowish white scaling papules in the margins. Similar lesions are on the upper part of the back. All fingers except the second one on the left hand show involvement of the nails, with thickening and piling up of debris under the nails. There is a bulbous appearance of the dorsal aspects of the terminal phalanges, especially of the perionychium. The eyebrows are almost entirely missing. In the mouth there is a whitish appearance of the hard palate, of the right buccal mucosa and at the corners of the mouth, where there is cracking and slight redness. All toe nails show thickening and have a yellowish appearance, with moderate yellowish scaling on all aspects of the toes. On the plantar aspect of the right heel there is dry thickening and scaling.

Direct microscopic examination of scrapings from lesions on the face, scalp and finger nails revealed the presence of myceliums and spores. Cultures from lesions on the face and from the scalp revealed a growth of both *Monilia albicans* and *Trichophyton purpureum*.

Sulfur and salicylic acid ointment has been used locally on the cutaneous lesions. On mouth lesions 2 per cent aqueous solution of gentian violet medicinal and a dilute solution of iodine have been applied locally. Riboflavin in 5 mg doses given twice daily has been taken with some temporary benefit. The patient had previously received from another physician thirty to forty injections of a mixture of dermatomycin and oidiomycin without benefit.

#### DISCUSSION

DR GEORGE K ROGERS, Phoenix, Ariz: I believe that the diagnosis is fairly well established, but I should like to suggest an examination of the stool for *Monilia* and a roentgenogram of the chest. I also suggest that the patient be given gentian violet medicinal by mouth.

DR M E OBERMAYER: I agree with the diagnosis of generalized moniliasis. Dermatologists are aware of the therapeutic difficulties which this infection presents. Experience has shown that a subthreshold diabetic background is frequently present in persons with generalized moniliasis. Even if a dextrose tolerance test should not reveal pronounced abnormalities, it seems advisable to put such patients on a low carbohydrate diet and to give small doses of insulin. A possible explanation is that the change in metabolism brought about by the injections of insulin makes the epithelial surfaces a poorer medium of growth for the yeast organism.

DR H J TEMPLETON, Oakland, Calif My first impression was that of solar dermatitis or lupus erythematosus I still think that the lesions have some connection with solar sensitization The "ids" may have localized in that particular area because of sensitization to sunlight

DR M F ENGMAN JR, St Louis I was particularly interested in this case because recently I have had 2 cases of generalized infection with *Trichophyton purpureum* in adults One patient was a man who had a mild generalized "eczema marginatum" type of infection in large patches The other patient was a sailor with a similar eruption, who told me that 40 men on his ship were affected I believe that generalized trichophytosis occurs with greater frequency than is realized and that in a number of such cases the disease remains undiagnosed This boy has a different type of eruption clinically He evidently has a *Trichophyton purpureum* infection of the scalp with secondary trichophytid in other areas The role of *Monilia* as a pathogenic organism in this case is open to doubt It seems to me that the burden of proof is on the person who claims that this is a mixed infection As to treatment, I should consider fever therapy Over twenty years ago Dr M F Engman Sr published some reports of cases of resistant ringworm of the scalp successfully treated with fever

CAPT ERVIN EPSTEIN (M C, A U S) I have had several cases of pulmonary moniliasis recently This fact inspired research studies in an attempt to discover the most efficacious antimicrobial agent In vitro experiments showed that dyes and iodides were comparatively ineffective The best agent according to these studies was thymol With regard to infection with *trichophyton purpureum*, this organism has been a common infective agent on the Pacific Coast The most effective therapeutic agent in my experience has been large doses of potassium iodide given orally

DR KENDAL FROST I second Dr Engman's suggestion that the burden of proof lies with the physician who diagnoses the coexistence of a double infection According to Lewis, the lesions of the two types of infection are usually separate when two types of fungi are found in the same person

DR HARRY P JACOBSON This is a most interesting case both from the standpoint of localization of the eruption and from the character of the double infection Localization of the eruption strongly suggests an element of photosensitivity The clinical history and the constitution of the patient point strongly to a nutritional deficiency as an underlying factor Whether this nutritional deficiency bears a causative relation to the double fungous infection or, per contra, a possible resultant toxemia from the fungous infection is responsible for the photosensitivity and the resultant localization of the eruption is, of course, not apparent In either event, I am of the opinion that the prime therapeutic consideration in the case should be an adequate supply of the vitamin B complex group and especially the nicotinamide fraction Suitable local therapy should be given proper consideration also

DR SAMUEL AYRES I appreciate the discussion I think it is possible that both organisms may be involved in this patient's infection, particularly at the time of his first visit, when he had lesions in the mouth characteristic of thrush *Monilia* was found in the mouth, but I do not recall finding *Trichophyton* there It has been particularly difficult to get successful results There is obviously a constitutional defect somewhere

## Disseminated Granuloma Annulare with Atrophy

Presented by DR NELSON PAUL ANDERSON

J A J, a woman aged 60, began to have the present eruption about seven years ago The first lesions were on the back of the left hand and on the neck The lesions on the hand have disappeared, and those on the neck have become much less noticeable The present lesions are located on the wrists, the upper outer surfaces of the arms, the anterior upper surfaces of the thigh and the popliteal fossae These are small to large erythematous and macular lesions with spreading circinate borders The lesions have slightly elevated edges There are numerous similar lesions scattered on the trunk The lesions on the upper part of the trunk and the lower part of the neck, both anterior and posterior, present a striking picture of superficial "tissue paper" atrophy

A microscopic slide presented with the patient reveals the characteristic picture of granuloma annulare This patient was presented before the New York Dermatological Society in January 1944

## Granuloma Annulare with Disseminate Lesions

Presented by DR CLEMENT E COUNTER

H M, a woman aged 53, began to notice an eruption on the thighs two years ago There has been little disagreeable sensation When she gets warm, the lesions tend to sting and burn The onset was on the occasion of wearing clothing suitable for a cool climate on an automobile trip to a warmer district She had been unable to adjust her clothing for the change in weather and continued her trip under the discomfort of being dressed too warmly From that time on the lesions on the thighs were persistent She has received ten intramuscular injections of bismuth subsalicylate Each dose consisted of 2 grams (0.13 Gm)

The present eruption is not as bright and defined as when first examined five months ago Individual lesions are about 4 mm in diameter These are smooth red papules, and they are arranged in groups of ten to twenty In some groups the arrangement of lesions is on the periphery of an irregular circular lesion from 4 to 6 cm in diameter All lesions are on the lower extremities except one, which is on the dorsum of the left hand over the fifth metacarpophalangeal joint This lesion is about 1 cm in diameter and is raised and red This lesion only is a fairly characteristic one of granuloma annulare

The microscopic picture of one of the small lesions on the right thigh revealed patches of cellular infiltration in the reticular portion of the corium There were epithelioid, lymphocytic and connective tissue cells No necrotic areas were present, and no giant cells or plasma cells

## DISCUSSION

DR GEORGE K ROGERS, Phoenix, Ariz I have a patient at the present time with similar eruptions on her legs The lesions have entirely disappeared after several doses of low voltage roentgen rays together with solution of potassium arsenite taken internally

DR JOHN GRAVES, San Francisco I have seen several patients in the past few years whose eruptions I thought might be thus classified On studying them further, however, we finally decided that they were not properly thus classified, particularly because of the histologic structure It suggested more the sarcoma type of reaction I finally came to the conclusion that there is no such thing as a disseminated granuloma

annulare, and now I have seen 2 patients in one day with that diagnosis

DR NELSON PAUL ANDERSON Dr Counter presented his patient because I encouraged him to do so, knowing that I was going to present one. I think that such cases of granuloma annulare, which one might call instances of a disseminated type of the disease, are interesting because they are so often mistakenly diagnosed. We used to associate this type of granuloma annulare only with adults, but at the present time I have as a patient a child with lesions on the eyelids, groins and buttocks which are typical of granuloma annulare. The atrophic lesions about the neck are not usually associated with granuloma annulare, but the textbook by Ormsby and Montgomery states that a considerable degree of atrophy is occasionally present in these lesions. I thought that this was an interesting case to present from the standpoint both of dissemination and of the presence of widespread atrophy.

DR CHRIS HALLORAN I have decided that cases of disseminated granuloma annulare are not so uncommon. We have seen 3 or 4 here in the last two years. The eruption in one woman at the Los Angeles County Hospital treated with bismuth cleared at first but recurred.

#### Contact Dermatitis Due to "Protek" Presented by DR A FLETCHER HALL

A woman, aged 32, employed in the manufacture of aircraft, for about one year has been working on outer wing assembly. She has used Protek on her hands during this period. There was no trouble with her skin until she noted a mild itching eruption of the hands on April 8, 1944. She then began to wear gloves, while still using Protek. Immediately the eruption became so severe that she had to quit work on April 17, 1944. Improvement since quitting work has been satisfactory.

The dorsal and lateral aspects of the hands, fingers and wrists are dry and pale pink, with ill defined rough scaling patches. The portion of the palms adjacent to the wrists have dried remains of intradermal vesicles. The treatment has consisted entirely of bland local applications. Patch tests with four of five items contacted by her at work elicited negative reactions, Protek alone elicited a positive reaction, and that appeared only after forty-eight hours, which was twenty-four hours after the test material had been removed.

#### Contact Dermatitis Due to the Resinous Ingredients of Zinc Chromate Primer and Certain Lacquers Presented by DR A FLETCHER HALL

R L, a woman aged 45, is employed as an aircraft worker. After drilling and filing zinc chromate-coated metals for ten months, she began to experience a mild but uncomfortable irritation of the skin of the lower part of her face and anterior and lateral aspects of the neck. This subsided in about three weeks, with the use of soothing local applications. Her occupation was changed, and since then she has been employed in sub-assembly, drilling, filing and handling bomb and torpedo release switch boxes, which are coated with black lacquer. Her eyelids and neck began to itch three weeks ago. This increased so that she quit work one week ago. She has swelling and edema of the eyelids. The front and sides of the neck show well demarcated, irregularly oval, discrete and confluent, pale pink, finely scaling plaques.

Reactions to patch tests with zinc chromate and black lacquer were negative both when the patch was removed and twenty-four hours later.

#### Contact Dermatitis Due to Pigment in Zinc Chromate Primer Presented by DR A FLETCHER HALL

C R D, a white man aged 68, is employed as an aircraft worker. Three months ago he began work burnishing "bright spots" on a zinc chromate-coated metal sheets. About two weeks later, a slight itching eruption appeared on his hands and wrists. He was then transferred to assembling "control boxes" and small control pulleys on rods, all of which were zinc chromate-coated. About two weeks ago a sudden flare-up of the dermatitis occurred. It was severe for one week, but there has been improvement in the past week, during which time he has worn gloves to protect his hands. Certain soaps have been irritating to his skin for many years. All aspects of the wrists and the dorsa of the proximal portions of the hands and thumbs show confluent erythematous squamous plaques, the borders of some of which are well demarcated.

A zinc chromate-coated disk applied as a patch test produced a positive reaction that persisted for five days. The height of the reaction occurred twenty-four hours after the patch was removed. Metal filings contacted by the patient produced negative reactions when applied as patch tests.

#### DISCUSSION OF CASES OF CONTACT DERMATITIS

DR H C L LINDSAY Protek is not a uniform product, I know of four different formulas for it. Some contain latex, and some contain soap. One that waterproofs and forms almost a glove contains latex. Others contain ivory soap flakes, glycerin, sodium silicate, tragacanth, oil of lemon and water, white wax, glyceryl monostearate, hydrous wool fat, sodium silicate (commercial solution), petrolatum and varying quantities of latex.

DR NELSON PAUL ANDERSON I believe that dermatologists are going to have to change their ideas as to contact dermatitis as to both its method of causation and its morphologic appearance, particularly eruptions due to the chromates and possibly nickel. Cases of patchy dermatitis are being observed which in ordinary circumstances would not even be considered as examples of contact dermatitis. Yet these eruptions become better when the patient stays away from work and become worse when he is at work. Many of these patients are not particularly intelligent, and this fact makes patch testing difficult. I have seen a number of Dr Hall's pictures of airplane workers. I feel that there is going to have to be a change of ideas as to what contact dermatitis is and how it is produced.

DR ANKER JENSEN I believe that dichromate dermatitis is a different type of eruption from ordinary contact dermatitis. If it had not been for the fact that Dr Hall had told me about some of these strange nummular types of dermatitis due to contact with the dichromates, I should have missed the diagnosis for a number of my patients. After talking to Dr Hall, I began to perform patch tests on these patients and found them sensitive to dichromate salts.

DR M E OBERMAYER I accept the diagnosis of contact dermatitis for the second case but not for the first and third cases. The eruption in the first case could not possibly be contact dermatitis if by that term



is meant an inflammatory process due to epidermal sensitization, such a process on the hands always involves primarily the sites where the skin is thin, such as the dorsa of the hands and the wrists, and has a tendency to be diffuse rather than to be present in the form of small plaques. In this patient the dermatosis involved primarily the palms, an anatomic site which because of the thickness of the epidermis, is notoriously resistant to epidermal sensitization. The suggestion that the eruption on the palms may be a secondary absorption dermatitis from lesions on the dorsa of the fingers also appears unlikely, these lesions were subsiding and could at this time not possibly be the cause of the active inflammatory lesions on the palms. I think that this patient has a dyshidrotic type of eruption of internal origin. In the third case there has been a chronic-recurrent dermatitis for sixteen years. The patient's mother had chronic eczema, and the patient himself is a tense nervous person of the worrying type. Symmetrically located, lichenified plaques were present on his legs. This man has dry neurodermatitis or lichen simplex chronicus, and the eruption on his hands is part of his disease. It is not unlikely that the substances with which he comes in contact in his work have a provocative influence, but that is not sufficient for labeling his cutaneous eruption contact dermatitis.

DR HAL FREEMAN I agree with Dr Hall's diagnosis as presented and I disagree with the speaker who says that a contact dermatitis must be continuous, especially one due to sensitivity to zinc chromate. That is what confuses a good many dermatologists. They are looking for the type of dermatitis described several years ago, in which there are no normal areas of skin in the parts involved, but in zinc chromate dermatitis, lesions are often defined, with areas of comparatively normal skin interspersed.

DR SAMUEL AYRES JR The woman with the dermatitis on the eyelids and neck did not have any positive reactions to patch tests with zinc chromate. She says that she has been using "42" hair oil. I have recently had a patient with a dermatitis from this preparation known as "42" hair oil. Apropos of Dr Schwartz's statement that persons who are sensitive to industrial irritants finally become toughened to them and have no further trouble, I should like to ask whether any one has ever seen patients who have experienced this.

DR W H GOECKERMAN I think that Dr Anderson's remarks are appropriate. The whole matter is complex. One often draws a too definite conclusion from a patch test. One has to deal with biologic problems. One speaks of an ordinary contact dermatitis too readily and feels that a diagnosis has been established with the demonstration of a positive reaction to patch tests. If this case could be followed through for a long time, such a diagnosis might be found incorrect.

DR A FLETCHER HALL I had wanted to bring some patients with eruptions characteristic of the two main types of zinc chromate dermatitis, but I could not get them to appear for the meeting, and so I did the next best thing—I brought 3 patients, each of whose cases had a "catch" to it. In the first case the woman had been wearing the same Protek on her hands for a year. A slight eruption developed, and she decided to wear gloves, then came the severe exacerbation. The lesions on the palms are undoubtedly dyshidrotic, and what the etiologic mechanism is I have no idea, but I have observed 10 or 12 cases

in which a worker with proved sensitivity had a typical contact dermatitis on the hands and wrists which became an acute dyshidrosis. I have seen dyshidrosis involving the hands and feet when there was no dermatitis near the feet. It seemed to be stirred up by a contact dermatitis elsewhere. As for the patient having a dermatitis on the backs of her hands, a patch test of whom was positive to Protek, I can not conceive of her contacting something over a period of a year to which she is 3 plus positive by patch test and then developing a purely coincidental dyshidrosis. She must have developed such a sensitivity shortly before onset of the eruption. The site of the patch test still shows faint pinkness and scaling after three weeks.

In the second case—the woman with the dermatitis of the eyelids and neck—the patient was unfortunately subjected to a patch test with the wrong resin by a nurse at the clinic. She is sensitive to alkyl resin (a phthalic anhydride) but not to bakelite resin, with which she was tested. This is her second attack. Last fall she was drilling and filing zinc chromate-coated material, she is no longer doing that but is drilling and filing switch boxes covered with black lacquer. Recently a change in specifications was made, requiring a coat of zinc chromate before the application of the lacquer, within a few days her dermatitis flared up. Because any of the resins in zinc chromate primer may cause a dermatitis like this, I think that one is justified in saying that this dermatitis is due to the alkyl resin.

Of the third case it should be stated that each patient who comes through the clinic at the aircraft factory is given a patch test with aluminum, duralumin and zinc chromate. In the testing of about 1,000 patients I have found only one false positive reaction to zinc chromate test disk. The oldest of my 3 patients today reacted strongly to zinc chromate. He is much better since wearing gloves for a week. The eruption of his wrists has changed from bright erythematous papular plaques to superficial faint pink scaling plaques. The fact that he has had eczema intermittently all his life is certainly no argument against his now acquiring a sensitivity to such a well known sensitizer as a chromate. A person with eczema is more apt to have such trouble than others. The dermatitis of the wrists is characteristic of the type which results from sensitivity to the chromate itself rather than to the resins. If he were sensitive to the resins also, his eyelids would probably be affected. The fact that the patches are sometimes well margined and have normal skin between them is characteristic of zinc chromate dermatitis. Such patches look like ringworm or nummular eczema and often are treated as if they were sometimes for months—before they are properly diagnosed.

#### Pseudoatrophoderma Coli et Corporis Presented by DR SAMUEL AYRES JR

A white woman, aged 35, has had an eruption of the back, chest, arms and neck for two years. This eruption has increased gradually in spite of local treatment with roentgen rays and the application of an ointment nine months ago. This eruption is now widely scattered over the chest, breasts, upper part of the abdomen, middle of the neck and outer aspects of the arms. The eruption is rather diffuse and dry. It consists of buff-pink fine scaly macules. In places these lesions are confluent. The skin over the whole body is dry. In addition, the patient has an extensive

and characteristic eruption of seborrheic scaling in the scalp and in the nasolabial areas. There is an appearance suggestive of a superficial atrophy in the lesions on the trunk. There is no apparent transfer of the eruption to other members of the family. One sister is known to have had an eruption from taking phenolphthalein. The microscopic examination of scrapings did not reveal fungi. A biopsy slide presented with the patient shows slight thickening of the stratum corneum with waviness of the epidermis. There is also slight thinning of the stratum mucosum and perivascular infiltration in the corium.

## DISCUSSION

DR H J TEMPLETON Shortly after Dr S W Becker wrote one of the early papers on this subject, I saw a patient with typical lesions, oval patches measuring 3 to 5 cm in length on the lateral border of the neck with a certain pseudoatrophic appearance. Some lesions had slight brownish scales, resembling tinea versicolor, but microscopic examination disclosed no fungi. The only point in which this case differs from mine is that the eruption was above the clavicle, while in mine all the lesions were below the clavicle.

DR KENDAL FROST A few years ago, I reported the cases of 2 sisters with similar lesions on the neck and front of the body. This woman also presents a patch on the back, which I think is parapsoriasis. Histologically, I think, one cannot tell the difference between parapsoriasis and pseudoatrophoderma colli. I brought out that point when I reported the cases of the sisters. I am not sure that this is a new disease.

CAPT ERVIN EPSTEIN (MC, A U S) In the 2 cases that I studied with Dr Frost and in the case that I presented before the San Francisco Dermatological Society several years ago, the outstanding clinical characteristic was a wrinkling of the skin of the affected areas. The lesions apparently improved after bathing, because the parakeratotic scales were removed. Those patients were younger than the one presented today. While no one has seen enough cases to define accurately the clinical variations that may occur in pseudoatrophoderma colli, I feel that the eruption of the patient seen today does not completely conform to the classic picture of the disease.

DR W H GOECKERMAN I have seen half a dozen cases over the years, and the lesions assume a variety of distribution and characteristics. The cause is unknown, neither does one know the cause of parapsoriasis, nor does one know whether all types of so-called parapsoriasis are of the same nature. The disease certainly presents a picture that cannot be put into any other category.

DR SAMUEL AYRES JR I thought that the case was worth presenting because of the rarity of the disease. In discussing the patients that Becker and Muir reported, Dr Becker said that he had observed a case in which the lesions had cleared after a vegetarian diet. Some one suggested use of vitamin A in large doses.

#### Multiple Benign Superficial Epithelioma Presented by DR NELSON PAUL ANDERSON

H L W, a woman aged 50, took a preparation of iron and arsenic for anemia over a period of three or four months about twenty-five years ago. She also took some medicine in the form of drops at about the same time. For the past fourteen years she has had

a red scaly eruption involving the lower part of the back. At the onset the eruption was diagnosed as psoriasis.

At present the palms present a few discrete but typical arsenical keratoses of the size of a small pin-head. On the lumbar region of the back are four or five large (dollar-sized) round erythematous, slightly scaly, sharply margined lesions. In one of the lesions is an elevated infiltrated mass the size of a large lima bean. There are dime-sized scaly psoriasiform lesions in the center of the chest.

A large elevated infiltrated basal cell epithelioma, the size of a half walnut, was present before its recent removal on the left temple. There was a lima bean-sized basal cell epithelioma just above the left eyebrow. Its center was depressed, and there was a typical pearly border. This lesion has been treated with radium.

A slide prepared from the biopsy specimen from the lesion removed from the left temple region was presented with the patient. It revealed a basal cell type epithelioma.

## DISCUSSION

CAPT ERVIN EPSTEIN (M C, A U S) I agree with the diagnosis as presented. I should like to mention another patient, that of a woman of 60 who had taken "drops" of unknown nature many years previously, a cancer developed in her right breast, and the breast was amputated. I saw her five years later, with four superficial basal cell epitheliomas of this type on her left breast and one in the scar of the right breast. The lesions had been diagnosed as psoriasis by several cancer specialists. The epitheliomatous nature of the lesions was confirmed by biopsy. This case is mentioned because of the association with deep carcinoma and because of the missed diagnosis, despite the typical clinical picture that is familiar to dermatologists.

DR. PHILIP K. ALLEN, San Diego, Calif I have recently encountered 2 similar cases, both with a diagnosis of psoriasis. It had been my impression that these lesions were fairly radioresistant, but in the second case there was satisfactory response to comparatively small doses of roentgen rays.

DR KENDAL FROST This case, as Dr Anderson brought out, is characteristically on an arsenical basis. There is a man in the ward at the General Hospital to whom I gave arsenic trioxide (Asiatic) pills in 1926. He appeared in the outpatient department a few days ago and said that he was still taking pills. He has no arsenical keratoses and no epitheliomas. I do not believe that every one who takes arsenic by mouth has these changes in the skin.

DR M F ENGMAN JR, St Louis The lesions on the lower part of the back appear clinically to be Bowen's dyskeratosis.

DR M E OBERMAYER I was especially interested to see that microscopically the lesions showed a cystic type of basal cell epithelioma, which I did not expect. As to Dr Frost's remark, I should like to point out that the potassium arsenite taken in the form of solution of arsenical keratoses and epitheliomas and not the arsenic trioxide of Asiatic pills.

DR NELSON PAUL ANDERSON This type of epithelioma has been more or less a hobby of mine for years. I feel that the majority of lesions of this type are due to a previous ingestion of arsenic. I do not think that the final story in this regard has been told.



A recent chapter was written by Drs Goeckerman and Wilhelm in the case of an elderly physician in whom cancer of the bladder eventually developed and he died. Tauber has reported instances of superficial epitheliomas in persons who have died of carcinoma of the lung. I do not believe it is possible for a person to take solution of potassium arsenite over a long period without suffering some ill effects. Every time cases of this type are presented the question of Bowen's dyskeratosis arises. If biopsy of the present lesions were performed, I believe that one would observe typical superficial extensions of basal cell proliferation extending into the cutis. In a certain percentage of such cases there occurs a certain large infiltrated tumor of a more or less soft type, which histologically is an adenoid type of basal cell epithelioma. I feel that the larger tumor masses are probably radiosensitive. I believe that the other flat lesions can be treated with roentgen rays or radium, but I see no reason for treating them in this manner. I think that they will respond well to solid carbon dioxide.

**Epidermolysis Bullosa Hereditaria** Presented by  
DR NELSON PAUL ANDERSON

N M, a woman aged 23, is one of 7 children. The father and mother are free of this disease. Two sisters have lesions, one of whom has only mild involvement. Two brothers are free of the disease, as are also two other sisters.

All the nails are absent except those of the fifth fingers, which are normal.

The extensor aspects of the elbows and the knees are covered with papyraceous scars. Numerous grouped milia are present on the anterior aspect of the left leg just below the knee. Both legs are involved in a widespread eruption consisting of numerous large bullae and large areas of erythematous and peculiarly glazed skin.

DISCUSSION

DR M T R MAYNARD, San Jose, Calif. This case is typical. The epidermal cysts are present on the left leg. I agree with the diagnosis.

**A Case for Diagnosis (Tumor of the Tongue?)**  
Presented by DR NELSON PAUL ANDERSON

M V H, a young married woman, about six years ago first noticed some dilated blood vessels on the right side of her tongue. At about the same time increased salivation developed, and she was unable to move her tongue freely. Salivation and stiffness of the tongue have improved recently.

On the right side of the tongue in its posterior half is a walnut-sized boggy swelling. This mass is peculiarly yellowish, and scattered over its surface are many dilated superficial telangiectatic blood vessels. In addition there appears to be a definite atrophy of the muscle fibers on the outer half of the right side of the tongue. This is seen especially well when the patient protrudes the tongue in the midline. When this is done, the tongue deviates to the right.

DISCUSSION

DR M T R MAYNARD, San Jose, Calif. There is atrophy. The patient stated that about twelve years ago she had a roentgenogram taken of a tooth on that side. The apparent atrophy has been going on for about six years. My suggestion is that she had an overdose of roentgen rays at the time the roentgenogram was taken.

DR NELSON PAUL ANDERSON. Has any one ever seen any such changes of the tongue in a person with paralysis of the hypoglossal nerve? The picture presented is certainly peculiar. I have not the slightest idea what the actual condition may prove to be.

**Adenoma Sebaceum** Presented by DR SAMUEL  
AYRES JR

J W, a white girl aged 10 years, until one year ago had had epilepsy of petit mal variety since the age of 3 years. During the past year she has had no epileptic attacks.

The present eruption began about three years ago and it has remained relatively unchanged since. The lesions are limited to the face and are especially numerous on the anterior and medial aspects of the cheeks. A few lesions are on the nose and on the chin. Much of the eruption consists of tiny capillary dilatations in the form of puncta. Diascopic pressure blanches the color. Some lesions are slightly elevated in pinpoint papules.

**Adenoma Sebaceum** Presented by DR SAMUEL  
AYRES JR

B M, a white girl aged 13, had convulsions from the age of 5 months to that of 11 months. Convulsions again occurred at scattered intervals until she was 3 years old. Later there were more convulsions when she entered school, but after five months of special schooling the patient had no trouble in attending school with other children. The eruption on her face has been present since birth. At first the eruption appeared to come and go, but in the last five years it has been persistent and increasing.

The patient is a normal-appearing girl, except for cutaneous lesions. The eruption is limited to the medial portion of the cheeks, the nasolabial folds, the nose and the chin. It consists of many closely crowded tiny bright red telangiectatic points. All lesions are pin-head size and smaller. They are flat-topped shiny papules.

DISCUSSION OF CASES OF ADENOMA SEBACEUM

DR M E OBERMAYER. The first of these 2 cases is an excellent example of the Pringle type of adenoma sebaceum. The diagnosis in the second case could not be established without biopsy. The lesions in this case are small maculopapules, level with the cutaneous surface, which left brownish-yellowish macules on diascopic pressure. Their lack of elevation and their brownish red color are suggestive of rosacea-like tuberculi of Lewandowsky.

DR H J TEMPLETON, Oakland, Calif. It is interesting to note that both girls were attaining good grades (B) in school.

DR ERVIN EPSTEIN (M C, A U S). A man from Los Angeles who had been given a diagnosis of adenoma sebaceum at a local clinic was recently drafted. He also had epilepsy and mild mental retardation. We made radiologic studies and found sclerotic areas in the skull. A diagnosis of tuberous sclerosis was made. It is suggested that the diagnosis of tuberous sclerosis be investigated for these 2 patients.

DR SAMUEL AYRES JR. I thought it interesting to see these 2 patients who are not related within a month. The only treatment I could think of is the destruction of individual lesions with electrodesiccation. When I saw the first patient the thing that impressed me was the telangiectatic appearance with vascular

points The history of epilepsy made it seem that the disease was a very early form of adenoma sebaceum

**Multiple Neurofibromatosis of a Peculiar Papular Form** Presented by DR KENNETH STOUT and DR M E OBERMAYER

H P, a man aged 29, has had von Recklinghausen's disease ever since he can remember His father had the same disease The patient was discharged from the Army in 1943 because of partial deafness This has also been present since birth There are typical lesions of neurofibromatosis on the neck, in the axillas and on the trunk A pigmented macular plaque on the left arm has remained stationary for many years Two years ago, when he joined the army, many flat papules of a different type appeared on his neck, chest and trunk, which have not undergone further changes

A light brown oval macular plaque covers most of the flexor surface of the left arm A number of soft, partly globular and partly filiform pedunculated tumors varying from a few millimeters to 1 cm in diameter, some of them hyperpigmented, are present on the neck, in the axillas and scattered over the trunk On the left side of the lower part of the back is a square plaque, several centimeters in diameter, which is studded with small papular, skin-colored lesions In addition to this eruption, there are a great number of firm, flat or lenticular skin-colored papules 2 to 3 mm in diameter, distributed densely on the nape of the neck above the clavicles, over the sternum and over the trunk The slide presented is from such a lesion on the right side of the chest The following paragraph is a description of the microscopic picture of the biopsy section

"The stratum corneum is partly loose and fluffy and partly parakeratotic, the stratum granulosum is one to two layers in thickness, the stratum mucosum is slightly dyskeratotic, and the basal cell layer is not sharply defined in places The dermis is made up of two kinds of connective tissue growth Close to the epidermis and only over a sharply circumscribed area are bundles of fine fibers and spindle-shaped cells, giving a compact appearance The rest of the tumor is composed of loose connective tissue fibers of a gelatinous consistency having spindle-shaped and round nuclei The blood and lymph vessels are dilated There is a narrow band of normal connective tissue between the gelatinous tumor and the epidermis, while the more compact growth blends with the epidermis"

#### DISCUSSION

DR H J TEMPLETON, Oakland, Calif The lesions around the neck would have to be differentiated diagnostically from the cutaneous tags of the neck which I described some time ago The extensive distribution and cafe-au-lait spots prove the diagnosis of neurofibromatosis

DR M E OBERMAYER I have never seen a patient with von Recklinghausen's disease in whom this peculiar type of papular lesions was present Some of these papules seem to be perifollicular, and when this patient was first seen I thought of the possibility of keratotic follicularis simultaneously present with von Recklinghausen's disease The clinical picture was further confused at that time because of intense itching and the presence of many excoriations within the involved areas It was soon found, however, that the pruritus and the excoriations were caused by infestation with scabies These lesions disappeared promptly after institution of therapy for scabies, while the flat peri-

follicular papules remained unchanged The lesions present two unusual features One is their clinical resemblance to keratosis follicularis, and the other is their appearance many years after the ordinary neurofibromas had become stationary On the basis of the microscopic examination, we believe that they are a rare variety of neurofibroma

### MINNESOTA DERMATOLOGICAL SOCIETY

S E SWEITZER, M D, *President*

H A CUMMING, M D, *Secretary*

*Minneapolis, May 12, 1944*

**Erythema Nodosum** Presented by DR S E SWEITZER, Minneapolis

J E M, a white woman aged 45, was admitted to the Minneapolis General Hospital on April 24, 1944, complaining of red nodules on the knees, ankles, elbows and ulnar surface of the forearms for the past six days The first lesions were noted on the knees, and these were soon followed by nodules on the ankles and elbows They became painful and tender and were firm to the touch She had a good appetite but was unable to sleep because of the pain In the past the patient was well except for epileptiform seizures occurring for the past fifteen years There was no history of ingestion of sulfathiazole She took  $\frac{1}{2}$  grain (0.03 Gm) of phenobarbital twice daily for epilepsy

Results of serologic tests for syphilis were negative Sedimentation rate was 70 mm in sixty minutes The percentage of hemoglobin was 79, the white blood cell count was 6,000, with 80 per cent polymorphonuclears, 13 per cent lymphocytes and 7 per cent monocytes The Mantoux test elicited a positive reaction Roentgenologic examination of the chest showed both sides of the diaphragm to be high The large vessels consequently assumed a transverse contour There was some calcification of the peritracheal nodes on the left, otherwise the chest was normal The electrocardiogram was normal except for tendency to left axis deviation

Examination showed numerous large and small indurated acutely red and painful round nodules in the skin and subcutaneous tissue These nodules were not sharply demarcated from surrounding tissue They varied from 1 to 3 cm in diameter and were located at the elbows, the ulnar surface of the forearms, the knees and the anterior tibial regions These nodules were warm to the touch and exquisitely tender There was great improvement after one week of rest in bed and sodium salicylate, 10 grains (0.65 Gm) four times a day by mouth

#### DISCUSSION

DR L H WINER, Minneapolis The patient had been getting phenobarbital daily since she was in the hospital, and the eruption improved In regard to the histologic section, the zones of necrosis surrounded by nests of eosinophils and numerous giant cells were noticed These changes were found not only in one area but throughout the whole slide One is accustomed to think of erythema nodosum as inflammatory when essentially a polymorphonuclear cell infiltrate together with decided edema is found

DR PAUL O'LEARY, Rochester Frequently when one believes, one stops thinking I believe that erythema

nodosum is a definite entity, but I do not believe that all acute inflammatory nodules on the lower extremities are necessarily erythema nodosum. In a study of lesions of this type, Dr. Montgomery and I believe that nodular vasculitis may simulate erythema nodosum and erythema induratum. The clinical differentiation is difficult and sometimes impossible, and the last histologic study may also need all the collateral evidence that can be collected to make a diagnosis of nodular vasculitis withstand critical analysis. We do not believe we have settled this issue, but the fact that occlusive vascular disease of the cutaneous vessels of the extremities does occur and that it is not due to tuberculosis or the streptococci seems to us a likely explanation for some of the cases of this type.

#### Macular Atrophy of the Buttocks Presented by DR S E SWEITZER, Minneapolis

O S, aged 55, was seen in the dermatologic clinic of Minneapolis General Hospital on March 25, 1944, complaining of multiple scars of the skin of the lateral lower quadrant of each buttock and an unhealed wound or sinus of the left buttock of two months' duration. The patient was treated for syphilis in 1940 by a private physician. She received three hundred and fifteen injections of bismuth preparations but no arsenic.

Serologic studies for syphilis gave positive results.

Examination showed many white macules on the lateral lower quadrant of each buttock and a healing sinus of the left buttock. Each macule was about 2 mm in diameter, depressed and atrophic.

Histologic sections were shown. In the section stained with hematoxylin and eosin the epidermis was atrophic and the papillary portion of the cutis was involved by perivascular infiltrate and degeneration of the connective tissue fibers. The section stained with Weigert's stain showed a diminution of elastic tissue in the papillary portion of the cutis of the involved area.

#### DISCUSSION

DR PAUL O'LEARY, Rochester: I agree with the diagnosis of macular atrophy.

DR L H WINER, Minneapolis: Dr. Sweitzer and I thought in presenting this patient that we might crystallize some opinion as to whether repeated needle punctures of intramuscular injections could cause minute scars that would show up as little white spots. This is a syphilitic patient who has had three hundred intramuscular injections into the gluteal muscles. On microscopic examination of the skin, we found that the elastic tissue in the papillary portion of the cutis was absent in these white areas. This change could be due to trauma of the needle puncture, but it is most likely due to punctate atrophy. I have not seen macular atrophy of so minute a nature as this.

#### Nodular Syphilid Presented by DR S E SWEITZER, Minneapolis

M S, a white woman aged 40, was seen at the Minneapolis General Hospital on April 27, 1944, with positive serologic reactions for syphilis. The past history revealed that she had secondary syphilis in April 1934, from which time to April 1936 she received fifty-seven injections of bismuth preparations and twenty-seven injections of neoarsphenamine. Her serologic reactions for syphilis reverted to negative within six months from the beginning of treatment and remained negative until 1937, at which time they again became positive. At that time the patient complained of dizziness

and fatigue, and examination of the spinal fluid revealed 33 cells per cubic millimeter, of which 23 were polymorphonuclears and 10 per cent monocytes. The protein content was 46 mg per hundred cubic centimeters, the Wassermann reaction was negative, the Kline reaction was doubtful 1 plus, and the colloidal gold curve was normal. She was given twelve injections of bismuth, after which she disappeared from observation. She was again seen at the Minneapolis General Hospital for correction of a fractured elbow in April 1944. At that time examination of the cardiovascular system and spinal fluid showed them to be normal.

Examination at the present time shows a well developed white woman with the arm in an airplane splint for correction of a fractured elbow. On the right posterior aspect of the neck are ten or twelve small nodules, 0.5 cm in diameter, of dusky red color, firm and slightly raised above the surface. On each side of the forehead and on the right forearm there is an isolated nodule which appears similar to those on the back of the neck.

Histologic sections showed endothelial vascular proliferation, with almost complete occlusion of the blood vessels. There was a dense perivascular plasma cell infiltrate in the cutis. The histologic examination corroborated the clinical and serologic diagnosis.

#### DISCUSSION

DR L H WINER, Minneapolis: Clinically this is tertiary syphilis, whereas histologically the lesion appears as secondary syphilis.

#### A Case for Diagnosis (Parapsoriasis?) Presented by DR S E SWEITZER, Minneapolis

H H, aged 48, was first seen at the Minneapolis General Hospital on March 24, 1944, at which time a coherent history could not be obtained because the patient was intoxicated and was suffering from a head injury. Roentgenologic examination at that time showed a fractured skull. There was clotted blood in the right ear and nostril. At this time there were multiple scaly, coppery colored lesions 3 mm in diameter on the trunk and legs, with a few on the arms. None could be seen on the scalp. There were eroded patches in the mucous membranes of the tongue and vagina. Examination of the spinal fluid revealed gross blood. Dark field examination of the eroded patches in the mouth and vagina did not show spirochetes. The patient was discharged on April 18, 1944.

Results of the designated serologic tests for syphilis were as follows:

March 24 Rytz and Kline, negative.

April 17 Rytz and Kline, Wassermann and Rytz specificity (at Minneapolis General Hospital), negative.

March 28 and April 14 (Serologic studies from Minnesota Department of Health) Kline diagnostic, negative, Kolmer-Wassermann 4 plus, acetone Kolmer, positive 4 plus, Kahn, negative, Eagle, negative, Hinton, negative.

Examination at this time showed brownish pigmented lesions on the thighs and legs and a few on the elbows. There were no mucous patches in the mouth or vagina. These lesions were 2 to 4 mm in diameter, with a shiny surface and coppery colored, and were sharply demarcated from surrounding tissue.

Histologic sections showed a hyperkeratosis of the epidermis with increased pigment in the basal cells. The cutis showed neither abnormal structures nor infiltrate.

## DISCUSSION

DR L H WINER, Minneapolis There are very slight changes in the microscopic section except for increased pigment in the basal cells This could be postinflammatory, but what preceded the present eruption I cannot say

DR L A BRUNSTING, Rochester It might be a late stage of urticaria pigmentosa

**Tinea Circinata** Presented by DR S E SWEITZER, Minneapolis

A P, a white woman aged 53, first noted a lesion on the right breast before December 1943 Previous to this, she noted itching of the right eyelid Within three or four weeks, another lesion appeared on the chest and others on the V of the neck, on the sides of the neck, on the arms, and on the lower part of the abdomen and the thighs They were intensely pruritic

Serologic tests for syphilis elicited negative reactions On repeated smear and culture, it was not possible to demonstrate fungi

Examination showed a lesion on the lateral aspect of the right breast 2 by 2½ inches (5 by 8.4 cm) with active periphery and healing center Smaller lesions, of the size of various coins, appeared on the V of the neck, the sides of the neck, the arms, the abdomen and the thighs All were scaly, were of a reddish lilac color and had more activity in the margins

Histologic sections were shown

## DISCUSSION

DR PAUL O'LEARY, Rochester Two diagnostic possibilities came to mind first, pityriasis rosea, and, second, a drug eruption Even though the plaques are of the type seen in pityriasis rosea it might be that the three pills she has been taking each night to make her sleep might be of etiologic significance

**Lupus Erythematosus** Presented by DR H E MICHELSON, Minneapolis

CASE 1—M S, a white woman aged 49, twelve years ago noted the development of lesions on her scalp which were associated with patchy loss of hair Two years later, small lesions appeared on her face They spread progressively in spite of topical therapy During the past year, some spontaneous regression of the eruption was noted The patient stated that exposure to sunlight aggravated the eruption

Examination showed scaling erythematous plaques on the cheeks, side of the face and eyebrow, with some atrophic scarring The scale was adherent and grayish In the scalp, there were several areas of total alopecia about 3 to 4 cm in diameter

Histologic sections were shown

CASE 2—E C, aged 7, was admitted to the University of Minnesota Hospitals on May 4, 1944 The mother first noted a lesion beneath the right eye three years ago At three to six month intervals, new lesions occurred on the scalp, face, upper part of the chest and back Many topical applications were used, but none influenced the growth or regression of the lesions The patient's mother stated that frequently the lesions had disappeared in the summer At no time did sunlight seem to aggravate the condition

The hemoglobin content was 11.7 Gm, the white blood cell count 5,200 and the platelet count 190,000 Culture of materials from the throat yielded hemolytic streptococci The sedimentation rate of the blood was 60

mm in sixty minutes and the temperature by rectum ranged from 98 to 100 F

At present, examination reveals scaly erythematous plaques, 0.5 to 1.5 cm in diameter, with depressed central portions covered with a grayish adherent scale The follicles in the lesions are dilated The lesions are located on the upper right side of the forehead, below the right eye and on the left parietal region of the scalp, left temporal region and left side of the chin There are depressed atrophic scars on the right aspect of the chest and over the right scapula

Histologic sections were shown The epidermis is atrophic and in places eroded The follicles are dilated and filled with hyperkeratotic plugs The sebaceous glands are also atrophic The upper part of the cutis is involved by nests of round cell infiltrate These cells are lymphocytes, plasma cells and phagocytes containing pigment granules The histologic observations corroborate the clinical diagnosis

## DISCUSSION

DR PAUL O'LEARY, Rochester I wonder if the combination of gold sodium thiosulfate and the various bismuth preparations that are now being employed in the treatment of lupus erythematosus is increasing the residual pigmentation of this disease It is now common to see a patient who has received both drugs either concurrently or in separate courses, and I have been impressed with the persistence and the extent of the pigmentation in these patients

DR S E SWEITZER, Minneapolis I think the pigmentation is more likely to come from the gold than from the bismuth

**A Case for Diagnosis (Epidermolysis Bullosa?)**

Presented by DR H E MICHELSON and (by invitation) DR JOHN M ADAMS

J P, a white infant aged 16 months, sustained a hot water burn to both legs on Dec 8, 1943 During the course, multiple bullae formed, and they have recurred seven or eight times in the past three or four months Pressure bandages and an Unna boot were tried without avail The bullae appeared to heal and then recurred with the formation of new bullae The father was said to have had milia and blisters around the toes during his childhood only, but he is now free from cutaneous disease In spite of an adequate intake of vitamin C, the blood level was found to be 0.1 mg on one occasion and 0.5 mg on another (normal 0.8 to 1.2 mg) Large doses of ascorbic acid were given by mouth The ascorbic acid level of the bullous fluid was 2.2 mg when the blood level was 2.0 mg

Examination shows extensive scar tissue with milia and bullae in the scars on both legs

## DISCUSSION

DR PAUL O'LEARY, Rochester The possibility of epidermolysis bullosa seemed less likely than a low grade infection in a burn scar The absence of bullae on the feet and other points of trauma, the localization of the blisters to the scarred area and the fact that the child had not demonstrated a susceptibility to trauma previous to the burn led me to believe that the burn and the therapeutic efforts explained the eruption rather than epidermolysis bullosa

DR S E SWEITZER, Minneapolis There is the possibility of epidermal separation taking place in the scar

DR L H WINER, Minneapolis We thought of epidermal separation, but in spite of use of an Unna boot, bullae developed underneath the dressing



mycosis fungoides one can say that it is acute when it is in the terminating stage, whereas if it is in a stationary condition it is said to be chronic. Although the first patient does not look any worse clinically than the second he has acute mycosis fungoides, whereas the second has the chronic form.

DR SHELDON STURMANS (by invitation) It is not feasible for any one to tell from the sternal aspiration that the bone marrow is clear. Not all the marrow is involved, and by the same token much of the skin is normal. I performed a biopsy of bone marrow for this man, and all I found was a myeloid hyperplasia with increase of plasma cells and histiocytic reaction which could result from any chronic cutaneous lesion. Elapsed time did not permit histologic sections of the bone marrow which might show something further, but the bone marrow that I have studied is absolutely normal. I think that the disease is a form of reticulum cell sarcoma, judging from the biopsy of the skin, and it manifests itself in the reticulum of the skin. Occasionally this lesion may set free tumor cells, producing a leukemic peripheral blood picture, then it closes and one never again observes this pattern in the peripheral blood. Imprints of these biopsies are uncertain.

#### Lymphosarcoma of the Nose Presented by DR S E SWEITZER, Minneapolis

I L, a white woman aged 78, was admitted to the Minneapolis General Hospital on March 19, 1944, complaining of swelling of the nose and obstruction to breathing for five weeks. The obstruction to breathing came first, and the involvement of the skin of the left lateral aspect of the nose appeared within one week prior to her admission.

Results of serologic studies for syphilis were negative.

On examination the patient showed a soft cystic annular disk elevated about 0.5 cm and about 3 cm in diameter on the left side of the nose. There was also a barely raised plaque of infiltration about 0.5 cm in diameter on the left ala of the nose. A third area of infiltration, about 0.5 cm in diameter, was present on the right ala. The left naris was obstructed by the mass, so that it was impossible to see whether the latter arose from the ala or from the septum. The mucocutaneous junction of the entire nasal orifice was infiltrated. Punch biopsy was performed, and microscopic examination showed a dense infiltration of lymphocytic cells, monomorphous in type. Numerous mitotic figures were evident, and a diagnosis of lymphosarcoma was made histologically. Roentgen rays in a dose of 750 r filtered through 1 mm of aluminum was administered to the lesion on April 20. Ten millicurie hours of radium was administered by needles in a mold inside the nose on April 18. Prompt regression of the lesion took place.

At present, examination shows a flat brownish pigmented area on the left side of the nose, the lesions having regressed rapidly in response to the radiotherapy.

#### DISCUSSION

DR L H WINER, Minneapolis This type of tumor is very susceptible to roentgen rays. It originates from lymphoid or tonsillar areas of the nose and throat.

DR STEPHAN EPSTEIN, Marshfield, Wis. Rapid appearance of lesions on one side and rapid disappearance following roentgen ray therapy is in general characteristic of lymphosarcoma. It seems to me that this feature is most evident in lymphosarcoma of the skin, both in primary and in secondary involvement.

Recently I had under observation a patient with a similar disease, a man 81 years of age. The lymphosarcoma apparently also originated in his pharynx. Within a few months numerous metastases, both cutaneous and subcutaneous, appeared that would melt away within a few days after roentgen ray therapy. Unfortunately, some of the lesions that show a rapid involution are ones that spread just as fast.

## CHICAGO DERMATOLOGICAL SOCIETY

I M WIEDER, M D, President

MARCUS R CARO, M D Secretary

May 17, 1944

#### Premycosis Fungoides Presented by DR HERBERT RATINER and (by invitation) DR MARTIN-EDMUND BROWN

C G, a white woman aged 55, has a generalized pruritic dermatitis which first appeared eight years ago and which has gradually increased in intensity.

The examination shows involvement of the back and chest, spreading more or less symmetrically. The eruption is red and sharply limited, with well defined configuration forming a plaque which is somewhat infiltrated and scaly. On the left breast the color is scarlet, and the infiltration is more intense. The biopsy was not revealing.

#### DISCUSSION

DR RUBIN NOMIAND, Iowa City I agree with the diagnosis. I think that the disease is a superficial mycosis fungoides, a type that is not particularly serious, runs a long course and will show only slight infiltration and slight atrophy in linear areas.

DR LOUIE H WINER, Minneapolis Clinically, I was interested in this patient because of the changes in the skin of the breast and the poikiloderma-like eruption. I think that the reason poikiloderma is not seen as it is described in the literature is that more diagnoses of premycosis fungoides are being made. This is not a case of premycosis fungoides, it is one of real mycosis fungoides. The eruption is multiform in character. One would almost get the idea that it is a form of lymphoblastoma.

DR HERBERT RATINER The case raises two interesting points. The first one is whether the plaque type of parapsoriasis invariably becomes mycosis fungoides and the second is what is the nosologic position of poikiloderma-like changes. Last month we presented a case of dermatomyositis with poikiloderma-like changes.

#### A Case for Diagnosis (Seborrheic Dermatitis?) Presented by DR E M SMITH JR

W J S, a white woman aged 52, presents a follicular eruption over the midline of the face which appeared after the use of a sun lamp. The eruption started on the forehead and has slowly spread down the face and around the nose. There are no subjective symptoms.

The patient is being treated for vasomotor rhinitis, consisting of nasal congestion, running of the nose and cough. She has had some loss of smell for twenty-seven years. She has occasional attacks of hives. She has had measles, whooping cough and diphtheria. Her tonsils were removed at the age of 36.

The Kahn reaction of the blood was negative. The examination of the blood showed hemoglobin level, 75 to 80 per cent, erythrocytes, 4,490,000, and leukocytes, 7,800, with 64 per cent polymorphonuclears, 1 per cent eosinophils, 30 per cent small lymphocytes and 5 per cent large mononuclears. The urine was normal. The basal metabolic rate was minus 15 per cent.

The roentgenogram of the left shoulder, taken because of an intractable pain in the middle of the left arm, revealed that that part was normal. The pain did not respond to salicylates. The physical examination showed normal conditions except for a slight mitral systolic murmur. The blood pressure was 120 systolic and 88 diastolic. She had the menopause one year ago.

#### DISCUSSION

DR STEPHEN ROTHMAN (by invitation) There was a conspicuous follicular hyperkeratosis and a fine telangiectasia with a sharp border, so I should hesitate to make a diagnosis of lupus erythematosus. There is no definite atrophy. I do not know what the disease is, but I think that it is not lupus erythematosus.

DR MARCUS R. CARO I hesitate to offer a diagnosis of seborrheic dermatitis, but because of the distribution and the only skin I should like to see sulfur ointment used, before accepting any other diagnosis.

DR L. F. WEBER I support Dr. Caro's suggestion.

DR E. M. SMITH, JR. We have made no diagnosis. I wonder whether any one has thought of Lewandowsky's tuberculid.

**Lupus Vulgaris** Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS

Miss A. M., an Italian-American woman aged 28, presents on the left elbow a silver dollar-sized plaque which is reddish brown, slightly elevated, of soft consistency and devoid of subjective sensations. On diascopic pressure there are typical minute apple jelly nodules. The eruption has been present for twenty-five years.

The histologic examination of a section removed showed involvement of the entire cutis, consisting of an infiltrate which was diffuse and composed of collections of epithelioid cells or nests with a sprinkling of lymphocytes surrounding these nests. Numerous giant cells of the Langhans type were seen below the epidermis and in the deepest area of the section. There was destruction of the connective tissue throughout the infiltrate. The epidermis was secondarily involved, presenting intracellular edema of the prickle cells with acanthosis and edema of the papillae with dilatation of the blood and lymph vessels.

The patient is still being examined for systemic involvement.

#### DISCUSSION

DR C. W. LAYMON, Minneapolis The thing that struck both Dr. Michelson and me was the wide diversity of the histopathologic picture. In one section there was definite caseation like that not infrequently seen in lupus vulgaris. In another section there was a picture of sarcoidosis, which brings up the point that lupus vulgaris histologically simulates every other type of tuberculosis.

DR D. V. OMENS The eruption which she presents on the face is the aftermath of a pustular infection on the face and scalp, which is now quite healed. She came in originally because of the eruption on the face and scalp, and only a week ago I noticed the lesion on the elbow. I took a section for examination, and the histologic structure was that of tuberculosis.

**Parapsoriasis** Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

Miss J. F., aged 21, presents a papulosquamous eruption of eighteen months' duration. The eruption first appeared on the thighs and has gradually spread to involve the trunk and upper extremities. The hands, feet, face and neck are not involved. The lesions are for the most part pea-sized discrete bilateral roughly symmetric raised oval papules, covered with a silvery scale which comes off *in toto* when scratched. There is no capillary hemorrhage. The eruption causes no subjective symptoms and has not responded to treatment with ointments.

**A Case for Diagnosis (Pityriasis Lichenoides et Varioliformis Acuta?)** Presented by DR. THEODORE CORNBLEET

S. L., a white boy aged 6 years, has had an eruption for two and one-half months which began on the neck while he had a sore throat and a cold and spread to the other parts of the body.

The lesions are on the trunk and extremities, the head is free. They consist of lichenoid papules with occasional vesicles. There is a superficial dry scale which in some places looks much like that of psoriasis. Some lesions dry to form crusts, and these fall, leaving pitted scars. The majority of the lesions leave only macules. There is little itching.

#### DISCUSSION OF THE PRECEDING TWO CASES

DR S. W. BECKER I believe that 1 patient has the chronic type and the other the acute type of pityriasis lichenoides.

DR MAURICE OPPENHEIM (by invitation) The little boy has typical pityriasis lichenoides et varioliformis.

DR LOUIE H. WINER, Minneapolis The first case is one of parapsoriasis. Comparing this case with the first case presented this afternoon, a history of itching was given in the latter but not in the former. If the histologic sections are compared, the one of the first case shows an infiltrate intermingled with basal cells so closely that a person cannot tell where the cutis ends and the epidermis begins. There is no sharp border. In the first case presented today there was a mycosis fungoides infiltrate which did not come up as close to the epidermis as it did in the other case. I think that the little boy has dermatitis herpetiformis.

DR S. ROTHMAN (by invitation) The second patient complained of itching. I think that itching is present at the very beginning of pityriasis lichenoides et varioliformis acuta. This is the same situation as that in lichen planus, for a widespread eruption and an inflammatory reaction are present. This inflammatory reaction may vary, and for this reason one should not put too much emphasis on it. I always ask the patient whether itching is present and whether his sleep is disturbed. If he has parapsoriasis, he may never be disturbed in his sleep.

DR THEODORE CORNBLEET I saw this boy for the third time today. Each time there were changes in the eruption. The outstanding feature of the eruption is that it does not have the same picture from day to day. I am sorry that the mother would not permit a biopsy to be made.

**A Case for Diagnosis (Acrodermatitis?)** Presented by DR. J. H. MITCHELL and DR. R. H. SCULL

B. H., a white woman aged 46, complains of an eruption that has been present for twelve years. It



began as red spots on the right arm. Later it involved both arms and the backs of the hands. There were no subjective symptoms.

On examination there was a reticular bluish red erythema, intermingled with red palpable nodules on the extensor surfaces of the right and left arms and to a lesser extent on the backs of the hands. Further clinical examination showed normal conditions.

The Kahn reaction was negative. A test with 0.1 cc of old tuberculin (1:1,000,000) elicited a positive reaction. The hematologic examination showed 45.5 per cent hemoglobin, 4,660,000 erythrocytes and 5,350 leukocytes. The urine was normal.

Two biopsy specimens were taken, one of a nodule and one of the macular erythema. The section from the nodule showed a thinning of the epithelium with a round cell infiltrate that was mostly subcuticular, perivascular and perifollicular in the upper part of the corium and with a fatty cell replacement in the deeper part of the corium. The second biopsy specimen, from the macular erythema, showed an essentially round cell infiltrate which was primarily perivascular.

#### DISCUSSION

DR F. E. SENEAR: Clinically, the woman had a great deal of acrodermatitis developing over the elbows. While my experience with acrodermatitis atrophicans chronica in the early stages is relatively limited, I do not recall ever having seen a patient presented with the disease limited to the arms. Whenever I have seen patients with the disease in the later stages, the eruption has been more diffuse.

It seems to me that the eruption is compatible with the edematous stage of acrodermatitis atrophicans chronica.

DR MAURICE OPPENHEIM (by invitation): This is a case of typical acrodermatitis atrophicans chronica. This papular eruption is observed not only in France and Austria but in the United States as well. It seems to me that it is regional. It is a disease in which one sees an edema with atrophy and a cigaret-paper-like thinning of the skin. On histologic examination there is round cell infiltration.

DR F. W. LYNCH, St. Paul: In the past this disease has not responded to therapeutic efforts. There is a recent report on the favorable action of sulfapyridine.

#### Multiple Superficial Epitheliomatosis Presented by

DR THEODORE CORNBLEET and DR HERBERT RATTNER

A man, aged 65, presents multiple epitheliomas. One in the right groin was recently removed surgically and was reported as being a squamous cell epithelioma.

#### Bowen's Disease Presented (by invitation) by DR S. ROTHMAN and DR A. SHAPIRO

T. B., a man aged 62, first noted a lesion on the small of his back about eighteen years ago, since then it has gradually increased in size. Itching is moderate. Four months ago a "growth" inside the lesion was excised by a physician. During the last week the lesion was treated with 5 per cent ammoniated mercury ointment, and this has removed much of the scaling. The patient was first seen in the University of Chicago Clinics on May 8, 1944.

The lesion is on the lower part of the back. It measures 18 by 12 cm and consists of erythema with dry lamellar scaling and crusting. The greatest part of the lesion is noninfiltrated, but there are irregularly shaped areas with superficial dermal infiltration. There

is a round atrophic scar, 2 cm in diameter, in the center of the lesion, at the site where the surgical excision was made.

The Wassermann and Kahn reactions were negative. On April 26, 1944, the erythrocyte count was 5,090,000, the hemoglobin content 17 Gm and the leukocyte count 9,400.

The patient has a duodenal ulcer, as verified by roentgenographic examination on May 1, 1944. The chest was normal on fluoroscopic examination.

The histologic examination showed the characteristic changes of Bowen's disease.

#### DISCUSSION OF THE PRECEDING TWO CASES

DR OLIVER S. ORMSBY: Bowen originally described 2 cases under the title of "precancerous dermatosis." In these cases the lesions were keratotic, flat nodules, arranged in a serpiginous configuration, resembling a nodular ulcerative syphiloderm. The lesions in these cases remained for several years without change. In a number of patients, whose cases have been described since that time, carcinomatous changes developed, hence the disease is really a carcinoma, rather than a precancerous dermatosis. A number of other conditions have since been described as Bowen's disease; they were multiple epitheliomatosis, erythematoid benign epithelioma or extramammary Paget's disease.

In 1925 Dr. Mitchell and I (Ormsby, O. S., and Mitchell, J. H. Multiple Superficial Epitheliomas, *ARCH. DERMAT. & SYPH.* 12:144 [July] 1925) presented a patient before this Society with multiple superficial epitheliomatosis who had a large number of lesions, particularly on the trunk. These lesions existed as dry, scaly patches like psoriasis for several years. The characteristic picture presented is a red scaly patch, having a threadlike pearly border and a moderately infiltrated center. In addition to this, nodules developed in one of the patches and later metastasized. The nodules presented features histologically of squamous cell epithelioma, the margin those of a basal cell epithelioma and the scaly center merely a dyskeratotic change.

In the benign epitheliomas described by Little (Little, E. G. *Brit. J. Dermat.* 35:435, 1923) there occurs a red scaly lupus-erythematosus-like patch with a fine, threadlike margin. Some of the superficial epitheliomas become moist and resemble lesions of extramammary Paget's disease. It can readily be seen from this that Bowen's precancerous dermatosis is very different from the other types mentioned and that it is a comparatively uncommon disease. The patient presented by Dr. Rothman today differs from one of this type and did not present the clinical picture of Bowen's disease.

DR S. J. ZAKON: The first case was studied at Northwestern University about ten or twelve years ago. In 1936 it was published as one of superficial epitheliomatosis by Dr. W. A. Rosenberg (*Superficial Epitheliomatosis*, *ARCH. DERMAT. & SYPH.* 34:973-979 [Dec] 1936). Four or five years ago the patient came back with a fungating mass in the groin which was shown to be squamous cell epithelioma.

DR CARL W. LAYMON, Minneapolis: On the left hand there were multiple keratoses. There were some on the palms and a few on the soles, and so the question comes up whether or not this man had ingested arsenic. It is believed that arsenic is a causative factor in certain cases of multiple epitheliomatosis, and it is Nelson Paul Anderson's opinion that many if not all patients with this disease have taken arsenicals at some time.

DR S J ZAKON We questioned the patient about taking arsenicals, and he said that he had not. He has worked all his life as a laborer on the railroad. By chemical studies we found no arsenic in the urine or the feces.

DR M H EBERT In connection with the discussion of arsenic as a carcinogenic agent in this case, some years ago I studied and published the results on the histologic examination of lesions that were left after an epidermal injection of neoarsphenamine given as a cutaneous test. In some of the patients the small nodules gave a histologic picture of Bowen's disease. I agree with Dr Ormsby that when dermatologists speak of Bowen's disease they should differentiate between Bowen's disease as clinically originally described and Bowen's disease as later described. Sulzberger has described Bowen's changes in lesions about the vulva.

DR THEODORE CORNBLEET This man had numerous seborrheic keratoses on the trunk, and the question came up whether they might be foci for some of these superficial epitheliomas, but actually at the site of the superficial epitheliomas there are but few seborrheic keratoses. While he does have some keratoses on the palms, he has no pigmentation which would indicate arsenical intoxication, though pigmentation need not necessarily be present for such intoxication. In these patients serious forms of cancer may sometimes develop.

DR S ROTHMAN (by invitation) I agree with Dr Ormsby that the case we presented is not typical of Bowen's disease. The lesion was more like that of epithelioma. The patient was first seen by a younger member of the staff, who thought that the man had psoriasis and prescribed ammoniated mercury ointment. When the patient reported to me, I thought it was a case of multiple epithelioma and performed a biopsy.

In regard to the growth in the other case, from the distribution I believe that it is a nevus.

**Lepra Maculoanesthetica** Presented by DR M H EBERT and (by invitation) DR M OTSUKA

H T, an unmarried Japanese aged 31, was born in California. At the age of 6 years he was taken to the Orient, where he lived for four years. He is unaware of any exposure to leprosy in the Orient or in this country. He worked at odd jobs, and in March, 1941 he joined the United States Army. One year later he was hospitalized with an infected left thumb. A skin graft was made, and while waiting for the "take" he noticed a numbness of the entire left thumb. A month later the little finger of this hand became numb. A few weeks later a silver dollar-sized reddish macule appeared on the left breast. He was hospitalized again, but the examination showed no evidence of syphilis or leprosy. However, he was discharged from the Army as a suspect leper and sent to the National Leprosarium in Carville, La., where he remained a year. He states that the lepra bacillus was never demonstrated in smears or biopsy specimens, but there has been no time to check his story officially. Wassermann reactions of the blood and spinal fluid were repeatedly negative. In March 1943 he was dismissed from the colony. Since then he has been working in Chicago, but he had to give up his work recently on account of weakness in his hands and difficulty in walking, in spite of injections by various physicians of thiamine hydrochloride, neoarsphenamine and bismuth. He had some sort of fainting "spell" about two weeks ago and was admitted to Cook County Hospital.

At present there are many well defined annular and macular lesions scattered over the anterior portion of the

trunk, upper part of back, hips and upper and lower extremities. These are round or oval and vary in size from that of a coin to that of a man's hand. When he was first seen, one week ago, he had a low grade fever and seemed much weaker than he does today, and many of the lesions had bright red borders. Today this condition has subsided, but the borders of some of the lesions are slightly erythematous. Many of the lesions are slightly infiltrated, giving the impression of edema. Other, older, lesions are slightly discolored and apparently atrophic and are covered with a fine scale. All these annular and macular lesions are anesthetic to pain and temperature. On the inner surface of the right heel there is a shallow ulcer the size of a half-dollar, with a dry black necrotic center and small bullae at the border. Over the right os calcis there is a large flaccid bulla without any surrounding erythema. There are three dime-sized healing bullae on the exterior surface of the left ankle and two on the plantar surface. The one on the left heel has a hemorrhagic border and a flaccid center. There are scars and relics of bullae on the palms. The head of the left epididymis is somewhat enlarged but not tender.

The extension of the proximal phalanges together with flexion of the distal phalanges produces a typical clawhand. The interosseus muscles are atrophic. There is some bilateral foot drop.

There is a paresis of the facial muscles, the patient is unable to pucker the lips, frown or close the eyes tightly. There is a coarse intention tremor in the facial muscles. The left knee and ankle reflexes are absent. Those on the right are exaggerated. There is a paralysis of the opponens pollicis muscles bilaterally with weakness of the interosseus and lumbricales muscles. There is glove anesthesia in the upper extremities and stocking anesthesia in the lower extremities to pain and temperature. The sensation of touch is retained. The ulnar nerves over the olecranon are enlarged and painless.

The Wassermann reaction of the blood serum was negative.

Histologic examination of a section removed from one of the edematous macules showed a cellular infiltrate made up of lymphocytes and groups of epithelioid cells around the sweat glands. Smaller foci of round cells and a few epithelioid cells were seen around the small vessels and nerves of the upper corium. A few acid-fast bacilli were demonstrated intracellularly within the endothelial cells of the capillaries in the subpapillary region.

Nasal smears and smears from the serum of the annular lesions were negative for acid-fast organisms. Acid-fast organisms were demonstrated in material taken by sternal puncture.

#### DISCUSSION

DR THEODORE CORNBLEET When I saw the patient five days ago, the lesions were darker and much more edematous than they are today. I wonder what could account for these changes.

DR OLIVER S ORMSBY This type of leprosy is a common one. I presented a case before this Society when the American Dermatological Association met here many years ago. That patient enlisted in the Army, was sent to Philadelphia, went from there to California and finally came back to Chicago. He had the typical anesthetic areas of leprosy. There were macules and bullae on different parts of the body. He had the peculiar misshapen hands. Histologic examination of a section removed showed the lepra bacillus. When I presented the case before the American Dermatological Association, Dr Montgomery, of California, and Dr

Fordyce, of New York, both agreed to the diagnosis of leprosy

DR M H EBERT The experience with leprosy is limited for most of the members here. This was impressed on my mind when some dermatologists from South America visited the clinic at Cook County Hospital. In every case they saw they suspected leprosy. The cases we see at the Cook County Hospital, which average about 2 a year, are of a mixed type, and the diagnosis is comparatively easy if one thinks of the disease. In this case the diagnosis was not difficult because the patient presents a clawhand. If one were to see the patient with just a single annular lesion, the possibility of leprosy might not occur to one. I think one should bear this disease in mind because our men in the armed forces will be exposed to leprosy in the Orient. According to Wengmueller, who wrote a long dissertation in the *Handbuch*, bullous lesions on the hands and feet should make one suspicious of the presence of leprosy. As in this case, some of them become secondarily infected and have a necrotic center, and they might well become stubborn ulcers. In the Medical Service the possibility of syringomyelia was thought of. Dr Lichtenstein made a careful examination of this man and said that there were three things that differentiated his disease from syringomyelia: the involvement of the facial nerve, the intention tremor and the nonsegmental distribution of the lesion. We were able to demonstrate the bacillus in the endothelial cells and superficial capillaries of the upper part of the corium.

#### Necrobiosis Lipoidica Diabeticorum Presented by DR MAURICE OPPENHEIM (by invitation)

W L, a white man aged 21, presents sharply limited, round and polycyclic contoured papules, from the size of a pea to that of a silver dollar on the external surface of both legs, on the dorsal aspect of the left hand and on the inside of the right arm. The surrounding skin is normal. The larger lesions show in the center sharply limited, round and oval contoured ulcers with punched-out margins and smooth sores, partially healed, and the size of a bean. The papules are yellow and light red, and on some areas there are a few telangiectases. The consistency is hard, like a grain embedded in the tissue, and the lesions are not painful to pressure.

The diabetes in the patient was discovered three years ago. One maternal aunt had diabetes. Three years ago the sugar in the blood was 298 mg per hundred cubic centimeters, and the patient was hospitalized. The cutaneous lesions appeared one year ago and have become worse despite the use of insulin.

#### DISCUSSION

DR S J ZAKON In 1 case I used insulin locally with good results. The idea is that the insulin will take care of the blood sugar, while the sugar in the skin will be retained for a longer period.

DR M R CARO In 2 cases reported by Dr Zeisler and me the intradermal injection of insulin into the lesions produced no change.

DR THEODORE CORNBLEET From a physiologic standpoint, that treatment seemed to me to be questionable. In the first place, a high value for sugar in the skin is directly reflected by that in the blood. Not much time elapses between the lowering of the blood sugar and that of the skin sugar. Secondly, the action of insulin does not take place in that manner, it has to take place systemically. I doubt that such therapy is indicated or that it would have effect on the lesions.

#### Urticarial Reaction from Penicillin (?) Presented by DR D V OMENS and (by invitation) DRS M OTSUKA and M S KAGEN

C S, a white boy aged 11 years, was in good health until three days before admission to the hospital on April 14, 1944, when he was kicked on the lateral aspect of the left knee. On roentgenographic examination there was no involvement of the bone. On the day before his entering the hospital, pain and swelling developed over the left tibia. On admission the patient had a temperature of 104 F and swelling, redness and heat over the middle third of the left leg. He was treated for an early osteomyelitis with sulfathiazole, 30 grains (1.94 Gm) immediately and 15 grains (0.97 Gm) every four hours thereafter. Despite therapy, the fever, leukocytosis and other symptoms continued.

On April 27, penicillin treatment was started, with about 50,000 units being given intramuscularly daily. On April 29, an incision was made, the infected area was drained and 400 cc of pus was obtained.

On May 3, 4 and 5, the penicillin treatment was discontinued due to the lack of supply, and the sulfathiazole treatment was restarted. On May 6, penicillin was given and continued without other medication until May 15, when an eruption appeared. Up to that time the patient had received a total of 790,000 units of penicillin.

On the morning of May 15, the patient complained of severe itching of the body, face and extremities. He was restless and scratched continually. Fingernail-sized wheals appeared over the entire body, and the lips and eyes became puffy. The administration of penicillin was stopped because of the reaction. On May 16 the symptoms were still present, so epinephrine hydrochloride and calcium gluconate were given to control the urticarial reaction. On May 17 the itching had greatly decreased, and many of the wheals had disappeared, although the swelling of the face remained.

The case is presented as an instance of urticarial reaction, possibly resulting from penicillin therapy.

#### DISCUSSION

DR S W BECKER Penicillin as marketed today is crude. Some crystalline penicillin has been used but mostly for clinical study. It is assumed that these lesions were not due to the penicillin itself but to the impurities which were present.

DR S ROTHMAN (by invitation) The boy had had sulfathiazole nine days previous to the onset of the eruption, so I assume it could be from the sulfonamide compounds. This could be decided by a passive transfer test, which consists in injecting serum from the patient and serum from a known normal person whose Wassermann reaction is negative into another person who is given a sulfonamide compound internally. An immediate reaction will follow in a hypersensitive subject.

I should like to ask Dr Becker whether acute or chronic reactions are seen from penicillin treatment.

DR S W BECKER There have been several types of eruption reported, varying from an urticarial toxic dermatitis to an exfoliative dermatitis. The eruptions are due to the impurities. There is no way of preventing them because there is not a sufficient amount of the material available.

DR HERBERT RATTLER I have seen a case of contact dermatitis from penicillin itself, not the vehicle. An Army medical officer who administered the drug shortly afterward acquired a severe dermatitis of the face, resembling a seborrheic dermatitis. Later there was an involvement of the hands and genitals. I ad-

ministered a patch test to him with the penicillin he was using and obtained a strong reaction. Then a patch test with some purified penicillin produced a 4 plus reaction, and later one with crystalline penicillin, obtained from the Department of Agriculture, also elicited a strongly positive reaction. The test with the liquor used as a vehicle elicited a negative reaction. This is a proved case of contact dermatitis from penicillin.

**DR D V OMENS** Because of the restriction on the use of penicillin, dermatologists have had very little experience with it. According to the history, this boy had no sulfathiazole except on May 3, 4 and 5, when penicillin was unavailable. He had no reaction until May 15, after he had had 790,000 units.

**Dermatitis Herpetiformis Treated with Acetarsone** Presented by **DR THEODORE CORNBLEET** and (by invitation) **DR D COHEN** and **DR H C SCHORR**

**F F**, a white man aged 60, has had an eruption for seven years. This is distributed on the extensor surfaces mostly, the shoulders, the buttocks and the trochanteric regions. The lesions are grouped and are mostly papules and vesicles. There is severe itching.

The patient has had various types of therapy without much change in the appearance of the eruption and without relief from the itching. Three weeks ago he was given acetarsone (250 mg). The first week he received 3 tablets, 1 a day for the first three days, the second week, 5 tablets, 1 the first day and 2 each of the two succeeding days, this past week he was given 2 tablets each of the first three days. Since the patient has been having this treatment there has been a striking involution of the eruption and the patient says that he has less itching.

**DISCUSSION**

**DR S ROTHMAN** (by invitation) On being questioned, the patient said that the itching was not much better. I think that most of us know that ultraviolet irradiation is good symptomatic therapy. If this were combined with the acetarsone, a more rapid improvement might be obtained.

**DR MAURICE OPPENHEIM** (by invitation) If acetarsone is used in the right way, it will give results. It is one of the arsenicals that is of value for pemphigus or dermatitis herpetiformis. Treatment with it should not be stopped too soon because a flare-up of the eruption will result. If the dose is increased, results will be obtained. Large doses of vitamin A might be given as a basic treatment along with the acetarsone.

**DR THEODORE CORNBLEET** One cannot measure the amount of itching which a patient has, except by watching his reaction and the effects on the skin. This patient said that his itching was considerably improved, though he still had some. As far as the eruption is concerned, there is considerable improvement. Even after the first week, when he had only 3 tablets, there was sufficient improvement to encourage us to continue the treatment. After the second week there was still more improvement, and there is really not much of the eruption left other than the pigmentation and some remains of lesions over the shoulders. I feel that for this particular patient acetarsone has been of service. He has had the eruption for seven years and has had experience with a number of other types of therapy.

**Periarteritis Nodosa** Presented by **Drs H E MICHELSON** and **L H WINER**, Minneapolis

**C G**, a man aged 37, was admitted to the hospital March 16, 1944, complaining of pain in the left side of the chest, a nonproductive cough, night sweats, aching

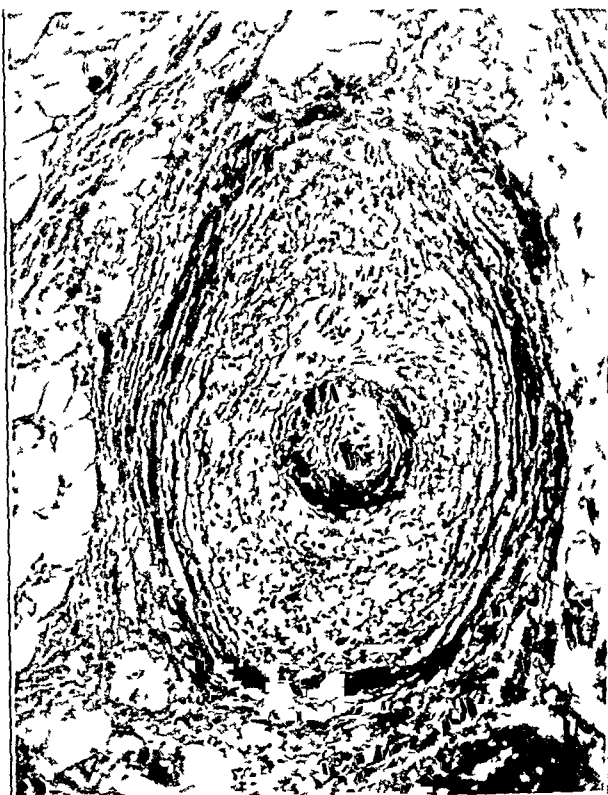


Fig 1—Low power photomicrograph of small artery, showing organizing thrombus and infiltration of vessel wall



Fig 2—High power photomicrograph of arterial wall, showing cellular infiltration and edematous degeneration of cells of the entire vessel wall

of muscles of the extremities and in the back over the renal region and stiffness of the leg muscles. All these symptoms were of one week's duration and became so severe in nature that the patient was admitted to the hospital.

On admission results of physical examination were normal except for a temperature of 100 F, pulse rate of 96 and respiratory rate of 20. The blood pressure was 106 systolic and 70 diastolic. The diagnosis on admission was a rheumatoid state or influenza.

His daily temperature went from 100 to 102 F, and his leukocyte count was between 17,000 and 18,000. He was treated with sodium salicylate until March 27, at which time the salicylates were discontinued and sulfadiazine was started. On April 3, pains developed in his chest, and the roentgenogram showed the presence of pneumonitis. The sulfadiazine was stopped on this date, and salicylate therapy again started.

The reactions of the Wassermann and all agglutination tests were negative.

On April 15, a large hard nodule was noted in the right axilla. Careful search showed small nodular masses on the lateral margin of the right tibia, apparently attached to the vessels, and one nodule was removed.

On April 26, penicillin therapy was started. The patient died on May 3, and autopsy showed:

1 Multiple aneurysms on the liver and on the small bowel. These were in the larger arteries (not the arterioles).

2 Infarct of kidneys

3 Hypertrophic left ventricle

4 Hemorrhage into the wall of the anterior descending coronary artery

5 Infarcts of the entire spleen

## PHILADELPHIA DERMATOLOGICAL SOCIETY

CARROLL S. WRIGHT, M.D., *Chairman*

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May 19, 1944

**Fungous Infection of the Back of the Neck** Presented by Dr. THOMAS BUTTERWORTH, Reading, Pa.

J. H., a white boy aged 15, presents an arciform ridge containing vesicopustules at the edge of a whitish plaque-like scar about 2.5 cm in diameter on the right nuchal region. A small active papule is situated nearby, where several other whitish plaque-like scars are present. The disease began about September 1939, as a small, nodular lesion on the right nuchal region, like an "infected hair." Tuberculin patch and intradermal tests gave negative results. The Kolmer and Kahn reactions of the blood were negative. Examination of potassium hydroxide preparations of hairs showed many spores and a few hyphae. Culture for fungi showed no growth after thirteen days. The patient has been treated with 12 per cent iodine in hydrous wool fats, equal parts of phenol and camphor, anthralin ointment (0.5 per cent), ointment and solution of benzoic and salicylic acid, sulfur-salicylic acid ointment, ammoniated mercury ointment and suberythema doses of unfiltered roentgen rays on four occasions.

## DISCUSSION

Dr. MORRIS MARKOWITZ: Tinea circinata would have to be severe to last so long. I am not sure that it is tinea.

Dr. SIGMUND S. GRIENBAUM: Is Dr. Butterworth satisfied with the diagnosis of fungous infection?

Dr. THOMAS BUTTERWORTH, Reading, Pa.: It was not my original diagnosis, and I was surprised when Dr. Weidman reported his finding of the fungus. I had even taken granuloma annulare into consideration. The patient visited me about once every six months over a period of years, but I cannot think of anything else. If there are any other suggestions, I should like to hear them.

Dr. SIGMUND S. GRIENBAUM: If fungi are present, this is probably a trichophytic granuloma in which the lesions are serpiginous rather than agminate.

Dr. THOMAS BUTTERWORTH, Reading, Pa.: Culture was ordered only two weeks ago, but until yesterday there had been no growth. The fungi are in the hairs, indeed, I think that most of the lesions have come in the parts covered by hair.

Dr. FRED D. WEIDMAN: It is not surprising that the lesions should appear on the glabrous skin as a result of recurrence. The hair is a reservoir, and, even though the lesions on the glabrous skin clear up, they can recur. Majocchi's granuloma sometimes develops in connection with ringworm of the scalp, and that results in scarring.

**Primary Inoculation Tuberculosis** Presented by Dr. CARROLL S. WRIGHT and Dr. ELMER GROSS

H. H., a white child aged 2 years, presents in the center of the left cheek an elevated papuloannular lesion about 1 cm in diameter. The color is reddish brown and persists under pressure with glass. In the left cervical region there is a lymph node the size of a hazelnut. In November 1943 a small round elevated lesion appeared on the left cheek and gradually increased in size. Shortly thereafter, an enlarged lymph node appeared in the left cervical region. The Mantoux test elicited a positive reaction. The patient has received three roentgen ray treatments of 150 r each, the growth becoming slightly smaller.

## DISCUSSION

Dr. D. M. SIDLICK: I saw this patient about three months ago. There was then no glandular involvement, but I made the diagnosis of lupus.

Dr. MORRIS MARKOWITZ: The border looks somewhat like that of juvenile epithelioma. A biopsy might confirm that diagnosis.

Dr. SIGMUND S. GRIENBAUM: I think that the lesion is tuberculous.

Dr. LOUIS GOLDSTEIN: Epithelioma can be ruled out because if the disease were epithelioma it would be either the prickle cell or the basal cell type, and the lesion on the cheek has no resemblance to the squamous variety of epithelioma. On the basis of the presence of an enlarged cervical lymph node, one cannot consider the basal cell type, which does not metastasize. I therefore agree with the diagnosis as presented.

Dr. SIGMUND S. GRIENBAUM: Is there a family history of tuberculosis?

Dr. CARROLL S. WRIGHT: I could not elicit any. We think that the child was infected from a contact.

Dr. REUBEN FRIEDMAN: There is a striking similarity between this lesion and those of another patient pre-



sented tonight, except that the boy's lesion is more erythematous

DR THOMAS BUTTERWORTH, Reading, Pa The family might be told that if a biopsy specimen is taken sometimes the whole lesion will disappear This has happened in my experience

DR CARROLL S WRIGHT I suggested the excision of a single nodule

### **Tuberculosis Cutis (?) and Psoriasis Presented by DR REUBEN FRIEDMAN**

E S, a white girl aged 6 years, presents on the left zygoma, left mastoid region, right nasolabial fold, right frontoparietal region, upper part of the back, epigastric region and right posterior iliac region a number of superficial sharply circumscribed waxy round or oval and slightly raised elevations, 0.7 to 1.3 cm in diameter Several have central granular depressions, giving to the lesions a pearly bordered appearance suggestive of epithelioma Others have thin silvery adherent scales In addition, there are a number of superficial circumscribed lesions with silvery white scales on the right frontoparietal region and right occipital hair line strongly suggestive of psoriasis The report of biopsy was as follows

"A considerable portion of the epidermis was ulcerated Its base was somewhat thickened by fibrous tissue Within this and extending almost to the subcutaneous fat, numerous milium tubercles appeared They were of such a strict epithelioid type that thoughts of sarcoid were entertained for a moment, but the abundance of giant cells within some of them, together with the ulceration, appeared to exclude this possibility In view of the clinical history, this is probably a case of disseminated milium tuberculosis"

#### **DISCUSSION**

DR D M SIDLICK On a clinical basis, I should consider this case as one of sarcoid Of course, the eruption could be tuberculous in nature, but I think that it is not frank tuberculosis

DR FRED D WEIDMAN I saw the sections and wavered between the diagnosis of Boeck's sarcoid and that of tuberculosis, with the balance somewhat in favor of tuberculosis If that were my child, I should want one of the nodules excised and its content inoculated into guinea pigs That is the only way to settle the question

DR JOHN F WILSON Is not the pathologic condition of the primary lesion rather nonspecific because of the lack of antibodies?

DR FRED D WEIDMAN No I should like to have Dr Callomon discuss that

DR FRITZ CALLOMON (by invitation) I believe that the disease is tuberculosis and not sarcoid I think it is tuberculosis miliaris faciei, the histologic section was, for me, convincing

DR REUBEN FRIEDMAN The patient has a palpable lymph node in the maxillary region at the angle of the jaw, and Dr Weidman called attention to palpable lymph nodes in both inguinal regions

### **A Case for Diagnosis (Lupus Erythematosus?)**

Presented by DR FRANCIS B EVELAND, Wilkes-Barre, Pa

S S, a white man aged 24, of good general appearance, presents a lesion on the forehead It is violaceous and nonatrophic, measures 3½ by 4½ inches (9 by 11.5

cm) and is sharply margined There are no subjective symptoms Similar lesions are present above and behind the ears There are four satellite lesions 1 cm in diameter with no alopecia There are approximately sixty nodules from the size of a pinhead to that of a split pea, scattered over the shoulders and arms There is regional adenopathy of the posterior cervical nodes There is a small lesion on the left cheek near the nose The Wassermann reaction of the blood was negative The family history was irrelevant There is neither tuberculosis nor cancer in the family The patient had had none of the usual childhood diseases He suffered from "indigestion" a few years ago, but in 1942 roentgen ray examination revealed that there was no peptic ulcer He has had an occasional cold but no other diseases of the respiratory tract The present eruption began about seven years ago with a lesion in the midline of the forehead A year later a lesion appeared above and behind the left ear Two years ago another lesion appeared above and behind the other ear Nodular lesions appeared on the shoulders last winter and increased to the present number

#### **DISCUSSION**

DR LOUIS GOLDSTEIN I think that this is a case of chronic disseminated lupus erythematosus The lesions on the forehead show atrophy and follicular plugging, while those on the shoulders are not of themselves distinctive of lupus erythematosus, in view of their violaceous color and their association with the other lesion, they may be part of the same process

DR CARROLL S WRIGHT I admit that I should have diagnosed the lesion on the forehead as lupus erythematosus, but those on the shoulder do not seem to fit in with that diagnosis

NOTE—Dr Weidman later reported on the histologic examination of sections from the back as follows Sarcoid can be definitely eliminated The general patterning was good for lupus erythematosus, with atrophy of the epidermis, dense keratotic plugging of hair follicles and a particularly dense perivascular round cell infiltration The cells in the latter, though, included elements other than lymphocytes and were not disposed on the usual loose, edematous reticulum, as is the case for lupus erythematosus There were numerous plasma cells, a few polymorphonuclear leukocytes and in numerous places epithelioid cells, the latter were never focalized into true tubercles Moreover, capillary blood vessels had consistently thickened walls, which were frequently disintegrated and were the seat of toxic hyaline degeneration All this speaks for an acute type of tuberculous reaction of the order that is exhibited in tuberculids Assuming that the specimen came from the back, one has an interesting combination of two reactions the one, lupus erythematosus, and the other, tuberculid This case may well represent one of those cases of lupus erythematosus of tuberculous origin in which the tuberculous basis is being signaled in the sections in a way that is usually not observed

### **Porokeratosis Presented by DR CARROLL S WRIGHT**

M K, a white man aged 49, presents lesions which first appeared fifteen years ago According to the patient, a biopsy was made at another hospital Past treatment consisted of roentgen ray therapy and injections The lower extremities are the sites of elevated verrucous lesions with elevated borders and depressed centers The encircling walls are brownish

## DISCUSSION

DR CARROLL S WRIGHT I saw this man about a year ago for about ten minutes and asked him whether he would be willing to come to a meeting at some time, but he never returned. In a year's time, owing to some patent remedies that he has been applying, the verrucous element has largely disappeared, but I still think that it is a case of porokeratosis.

DR FRED D WEIDMAN This is as clearcut a picture, clinically, of porokeratosis as I have ever seen. I have objected several times to the concept that one must be able to see with the naked eye the central fissures in the ridge around the lesion. Several patients have been presented at these meetings with what I thought was porokeratosis, and a real discussion hinged around that point. In the "Corpus Iconorum Morborum Cutaneorum" there are some photographs in which one can see the fissures and others in which one cannot see them.

#### Xanthoma, or Lipid Disturbance Presented by DR CARROLL S WRIGHT and DR ELMER GROSS

R S, a white boy aged 4 years, presents numerous yellowish pea-sized and larger papules, chiefly on the face, elbows and knees but more or less generalized. In areas where involution has occurred, there are pigmented macules. When the child was 10 months old a generalized eruption of discrete papules and vesicles developed. The color of the papules has always been yellow. Many have undergone involution, but the face, elbows and knees still show numerous papules. The serum cholesterol level was 295 mg per hundred cubic centimeters. The patient has been given a low fat diet.

## DISCUSSION

DR FRED D WEIDMAN I agree with the diagnosis of juvenile xanthoma. For a long time I have held the opinion that a good many xanthomatous changes are simply superimposed on previous lesions, as in the case of scar xanthomas. In its simplest expressions, various kinds of scar will become xanthomatous, but the basis may not quite amount to a scar, as in the case of the original locus of erysipelas. I inquired of the mother whether any of the lesions had ever been present without being yellow, and she said "yes." I have looked back trying to discover whether the child has ever had something else, for example, a fibroma which has become xanthomatous. I think that not all these lesions have at one time or another been yellow. It may be that more exhaustive inquiry into the history may show that they have been, but I have failed in the attempt tonight to get that history.

DR CARROLL S WRIGHT About two years ago I presented a man who had the same picture and whose lesions disappeared after he had been on a low fat diet for three months.

DR FRED D WEIDMAN Dr Butterworth has had success with a low fat and low carbohydrate diet.

DR THOMAS BUTTERWORTH, Reading, Pa Low fat and low carbohydrate plus insulin. Dr Markowitz has just told me that a patient whom he presented some months ago did well with that treatment.

#### Necrobiosis Lipoidica Without Diabetes Presented by DR THOMAS BUTTERWORTH, Reading, Pa

G W McK, a white woman aged 35, presents shiny, glistening hand-sized yellowish plaques on the anterior aspects of the legs. The borders of the lesions are purplish. Many telangiectases course over the surfaces

of the plaques. The cellophane-like appearance is striking. For about three years she has had an asymptomatic eruption on the anterior aspect of each leg. Her past history reveals nothing essentially significant. Her mother and father both had diabetes, and her brother now has diabetes. The patient is overweight and suffers from chronic hypotension. The urine was normal, and the blood sugar level 72 mg per hundred cubic centimeters.

#### Necrobiosis Lipoidica Without Diabetes Presented by DR THOMAS BUTTERWORTH, Reading, Pa

P D, a white woman aged 34, presents a triangular yellowish plaque with a cellophane-like, glistening appearance about 6 inches (15 cm) below the left knee on the anterior aspect of the leg. The border of the lesion is violaceous, and many telangiectases course over the surface. Several yellowish red patches farther down the leg are probably early lesions. The lesions appeared on the leg early in 1942. Her past history and family history are noncontributory. The value for a complete blood count, the urinalysis and the basal metabolic rate were within normal limits. On March 7, 1943 the blood sugar level was 75 mg per hundred cubic centimeter. On May 1, 1944 the dextrose tolerance test of a fasting specimen gave the following values: fasting, 81 mg, after half an hour, 164 mg, and after one hour, 170 mg. On April 24, 1944, the blood sugar level was 94 mg and the cholesterol level 119 mg per hundred cubic centimeters.

## DISCUSSION OF THE TWO PRECEDING CASES

DR THOMAS BUTTERWORTH, Reading, Pa I have done nothing in the way of treatment. The family history in the first case is interesting, both parents and a brother have diabetes. For the other case there is a dextrose tolerance curve which would probably be called high normal. I think, therefore, that I shall have to watch these patients every six to twelve months to see whether they eventually have diabetes.

#### Schamberg's Progressive Pigmentary Dermatitis Presented by DR THOMAS BUTTERWORTH, Reading, Pa

G T S, a white woman aged 19, presents a brownish red eruption on the inner and outer sides of the ankles which gradually fades as it approaches the middle of the legs. On the involved areas there are many cayenne-pepper-like puncta. The eruption began on the feet last summer and has gradually extended upward to the middle of the legs. None of the involved areas have shown any tendency toward clearing.

## DISCUSSION

DR CARROLL S WRIGHT I have seen only 1 case which Dr Schamberg said presented the correct picture.

DR MARGARET MAYNARD, New Orleans (by invitation) This disease is common in the South. I have never before seen it in a woman—always in men.

DR CARROLL S WRIGHT In this case tonight I could not find the paprika spots characteristic of the disease.

DR A STRAUSS I once presented a girl with this disease who did a lot of horseback riding, and Dr Schamberg concurred in the diagnosis.

DR FRANCIS B EVILAND, Wilkes-Barre, Pa I do not know what else this eruption could be, but a few years ago Dr Klauder presented here a case of an eruption which was called "Schamberg's disease" and in which there were little satellite bright pepper-ree



lesions New lesions would start from the old, and so on I did not see them in this case, but I do not know what else this case could be

DR FRED D WEIDMAN There are forms of purpura which could look like this eruption The patients are candidates for studies of clotting and coagulation time of the blood, platelet counts and other studies of that sort to determine whether there is anything in the blood to explain a purpuric eruption Dr Schamberg told me that in a case that he had studied there was a high blood cholesterol level

DR CARROLL S WRIGHT That is true, I have seen 2 patients, both of whom had a high blood cholesterol level

DR MORRIS MARKOWITZ A biopsy may help, it may show deposits of iron pigment in the tissue

#### A Case for Diagnosis (Pustular Bacterid?) Presented by DR THOMAS BUTTERWORTH, Reading, Pa

L E C, a white man aged 50, exhibits palms and palmar aspects of the fingers that are thickened scaly and fissured A few pustules are scattered over the palms The fingers are held in semiflexion, and motion is definitely limited Erythemasquamous patches with slight fissuring are present on the left heel and behind the left little toe The finger nails are extremely irregular and pitted The patient had ulcerative colitis in 1932 His finger tips became fissured in 1932 Since 1939 he has had an erythemasquamous rash on the palms, palmar aspects of the fingers and the heels Within recent years successive crops of pustules have developed on the palms Extensive studies in a naval hospital in 1939 were inconclusive as to diagnosis Repeated roentgenograms of the teeth showed them to be normal The nasal sinuses are clear, and the tonsils have been removed Prostatic examinations were normal The patient has lost approximately 16 pounds (7 Kg) in weight since 1939

A urinalysis gave normal values A complete blood count showed only a moderate secondary anemia A gastric analysis showed the fasting value for free hydrochloric acid to be 19 degrees and for total acid 25 degrees After a test meal the value for free hydrochloric acid was 40 degrees and for total acid 56 degrees The Kahn and Wassermann reactions of the blood were negative The blood sedimentation rate was 9 mm at the end of one hour The blood sugar level was 82 mg, the blood cholesterol level 270 mg and the blood urea nitrogen level 12.5 mg per hundred cubic centimeters The icterus index was 8 Material obtained by drainage of the gallbladder yielded a profuse growth of *Bacillus coli* in Endo medium Culture of a pustule on the palm showed gram-negative diplococci and nonhemolytic streptococci Repeated scrapings of the skin have not shown fungi

Sulfathiazole ointment applied locally has given most relief Iron and arsenic, aluminum hydroxide gel and phenyl salicylate and extract of liver have been administered by mouth Biliary drainages with a solution of neo-silvol (1:5,000) weekly are being carried out by a gastroenterologist

NOTE.—This patient responded remarkably to treatment with 5 per cent sulfathiazole cream applied locally and sulfapyridine administered by mouth Earlier the administration of sulfathiazole by mouth had not been helpful

#### DISCUSSION

DR HERMAN BEERMAN This patient reminds me of a Negro recently shown here for whom the diagnosis of lupus erythematosus was subsequently made

DR FRED D WEIDMAN This patient, in addition, has a hyperkeratosis of the heel, attended by fissuring They are not simply callosities Since pustules are absent tonight, I inquired particularly about them, and the patient said that he had had them and that from these one could actually secure pus If I were to attach full weight to what the patient says, I should regard this eruption as pustular bacterid

DR CARROLL S WRIGHT I think that this is another of those eruptions like acrodermatitis atrophicans chronica of Hallopeau, which dermatologists discuss without really knowing what they are talking about

DR FRANCIS B EVELAND, Wilkes-Barre, Pa I wondered about the sclerodactylia shown by this patient

DR CARROLL S WRIGHT That apparently disappears when the eruption is in a state of quiescence I think that it is a secondary effect

DR SIGMUND S GREENBAUM When one finds streptococci in a lesion of this sort, that fact excludes the diagnosis of bacterids does it not? In any event, the lesions described by Andrews as bacterids were sterile

DR THOMAS BUTTERWORTH, Reading, Pa The only infection which the patient has had is an infected gallbladder Even before the report of infection with a non-hemolytic *Streptococcus* was made I thought of pustular bacterid as a possible diagnosis, but nothing we had done for him had helped much, hence I applied 5 per cent sulfathiazole ointment, and that gave him more relief than anything else

DR LOUIS GOLDSTEIN There was a recent article by Walter Lever (*ARCH DERMAT & SYPH*, 49:273 [April] 1944) on the favorable effect of internal administration of sulfapyridine in a case of acrodermatitis continua of Hallopeau I wonder whether it would not be worth a trial

DR SIGMUND S GREENBAUM Assuming that it is an infectious process, one might try the local use of the filtrate of *Bacillus brevis tyrothricin* It is marketed by Sharp & Dohme, Inc

#### Steatocystoma Multiplex Presented by DR THOMAS BUTTERWORTH, Reading, Pa, and DR EDGAR BEIDELMAN, Bethlehem, Pa

J A P, a white man aged 26, presents whitish and chamois-colored papules and nodules on the trunk and upper parts of the thighs The lesions are most numerous in the presternal region, the axillas and the lower part of the abdomen When the lesions are pierced, a creamy substance resembling toilet wool fat may be expressed The lesions appeared first on the sternum when the patient was 12 or 14 years old

#### DISCUSSION

DR SIGMUND S GREENBAUM Some of the lesions have a reddish tint

DR HERMAN BEERMAN Some years ago I presented a Puerto Rican with a similar eruption (*ARCH DERMAT & SYPH*, 31:154 [Jan] 1935) Some of the lesions get secondarily infected and become red After they are punctured, a clear oil escapes A series of articles by Shields Warren and his associates in the *American Journal of Pathology* (19:441, 591 and 765, 1943) deals with the subject of tumors of the dermal appendages

DR SIGMUND S GREENBAUM Do you think that the redness is inflammatory?

DR HERMAN BEERMAN Yes, ordinarily the lesions are not inflammatory

DR FRED D WEIDMAN The redness is a foreign body reaction—a granulomatous reaction against foreign fats

DR SIGMUND S GREENBAUM How is that different from the ordinary sebaceous cyst?

DR FRED D WEIDMAN In no way at all. Sebaceous cysts exhibit foreign body reactions when the lining epithelium becomes atrophic or otherwise destroyed

**A Case for Diagnosis (Achromic Nevus, Atypical Hydroa Puerorum?). Presented by DR THOMAS BUTTERWORTH, Reading, Pa**

A R S, a white boy aged 5 years, presents a whitish macular eruption involving the pectoral region, shoulder and deltoid area and extending halfway down the scapula on the right side. There is no surrounding hyperemia or pigmentation. Friction produces bright erythema. The parents were asked to expose the child to the sun for one or two days before this presentation, in an attempt to produce vesiculation. The child's skin appeared normal at birth. At the age of 3 years he was exposed to the sun, and "blisters" developed on the top of the right shoulder. Each summer, whenever he has been exposed to the sun, vesiculation has occurred on a larger area. During the winter months the skin is smooth. The parents are not related

DISCUSSION

DR THOMAS BUTTERWORTH, Reading, Pa. Some authorities separate the achromic nevus anemicus into one type in which there is vascular deficiency and into another type in which there is a nevusoid absence of pigment. I have never seen "blisters" on this child, but the mother promised to get him into the sun so that he would have the bullous lesions. If the skin of the child blisters, perhaps they are of the achromic type rather than of the anemic

DR SIGMUND S GREENBAUM But why call it a nevus if the patient gets "blisters" from the action of the sun?

DR THOMAS BUTTERWORTH, Reading, Pa. I can only call attention to the macules. I thought at first that it was nevus anemicus, but when I heard of the "blisters" I began to consider hydroa puerorum

DR A STRAUSS I should call this leukoderma—a nevus of the achromic type rather than of the anemic

DR FRED D WEIDMAN I take it that there is no question about the boy's having had blisters, the parents stated that he had blisters, and any layman knows a blister. I do not know why we are discussing nevus in the case

DR THOMAS BUTTERWORTH, Reading, Pa. Because of the unilateral character. My reason for changing the diagnosis to the achromic type was that the skin did blister, but I wanted to see the blisters

DR A STRAUSS I should consider vitiligo rather than nevus

DR FRED D WEIDMAN But that diagnosis does not tie in with blisters. Has familial benign pemphigus been considered? This disease shows blisters, but I have not heard of scarring

**Idiopathic Gangrene of the Penis Complicating Scabies Presented by DR L E McCRAE (by invitation) and DR REUBEN FRIEDMAN**

H H, a white man aged 26, about a week or two following an alcoholic-sexual debauch, had a generalized itching eruption which also involved the penis. About

two months later, on April 18, 1944, he noticed that his penis was beginning to swell. The swelling became rapidly and progressively worse, and on the following afternoon he was admitted to the hospital. On admission the entire shaft of the penis was greatly swollen, with a maximum thickness of from 2½ to 3 inches (6.3 to 7.6 cm) in the coronal region. A large black gangrenous sloughing area was present distally. There was no urethral discharge. Bilateral inguinal adenitis was present. The gangrenous process spread rapidly, involving practically the entire shaft. Aerobic and anaerobic culture revealed a few staphylococci (*Staphylococcus aureus*) a moderate number of nonhemolytic staphylococci (*Staph. aureus*) and a few streptococci (*Str. viridans*). The Kolmer, Wassermann, Mazzini and Kahn reactions of the blood were negative. A complete blood count made on the patient's admission to hospital showed hemoglobin content, 82.6 per cent, erythrocytes 4,480,000, and leukocytes 18,000, with 86 per cent polymorphonuclear leukocytes, 12 per cent lymphocytes and 2 per cent monocytes. The color index was 0.92. The pathologic diagnosis was chronic inflammatory reaction. The patient received sulfadiazine therapy from April 23 to April 30, 1944, inclusive

DISCUSSION

DR FRITZ CALLOMON (by invitation) This interesting genital lesion corresponds to the disease described by Scherber and Muller in the twenties as "balanitis erosiva circinata et gangraenosa". The inflammatory changes associated with necrosis resemble strikingly those shown in the colored photograph published by Scherber in Jadassohn's *Handbuch* (vol 21, p 227). Only the coexistence of the two symbiotic microorganisms was responsible for the pathologic changes, the significant "fusospirillosis" apparently was not demonstrable in the case under discussion tonight. The scabies may have changed the situation. Scherber described this fusospirillosis as identical with the findings in smears from Vincent's angina. The close relationship between the two diseases and the occasional origin of the genital lesion from tonsillar, buccal or gingival ulcers of Vincent's disease have been described by Cirillo, Milian, Queyrat and McCormac (cited by Scherber in Jadassohn's *Handbuch* and in my textbook on the nonvenereal diseases of the genitals [G. Thiem, Leipzig]).

As to treatment, it was noted that sulfadiazine was used. I have had no personal experience in the treatment of Vincent's angina and similar lesions with sulfonamide drugs. However, if sulfonamide drugs have been effective against the oral disease, one may be justified in expecting a similar effectiveness against the corresponding genital infection. In any case, when given, sulfonamide drugs should be administered both externally and internally. Scherber found local treatment with hydrogen peroxide most successful after the lesion had been opened, recovery tended to be more rapid after release of tissue tension, free access of air and local treatment made possible by a large incision of the phimotic prepuce.

DR REUBEN FRIEDMAN The sulfadiazine was given only internally in this case

DR THOMAS BUTTERWORTH, Reading, Pa. Did the patient have much secondary infection with his scabies?

DR REUBEN FRIEDMAN No. No Vincent's organisms were found. The patient was given neoarsphenamine on several occasions and then its use was stopped. He improved with simple applications of boric acid ointment, and the lesion is now granulating nicely. The

only treatment which the patient had for his scabies was self administered. The disease was undiagnosed, and the only treatment employed for two months before the onset of the gangrenous process was bismuth-formic iodide compound powder.

DR THOMAS BUTTERWORTH, Reading, Pa. A method of treatment, not immune to criticism, which my colleagues and I employ at an institution for feebleminded patients is to incorporate sulfathiazole with peruvian balsam and sulfur. The pyoderma disappears with the scabies. Years ago oxyquinoline sulfate was used in conjunction with sulfur. This worked better than sulfur and peruvian balsam alone, but since their advent sulfonamide compounds have been substituted.

DR REUBEN FRIEDMAN. Dr Callomon suggests that the treatment for scabies affected the findings of the Vincent's organisms, however, the treatment for scabies was not instituted until about two weeks after the patient was in the hospital. It was not diagnosed until after consultation with the dermatologic department for interpretation of the generalized eruption.

DR SIGMUND S. GREENBAUM. A significant feature is the rapidity with which the gangrenous part resolved. In six or seven days the gangrenous parts literally dropped off.

DR REUBEN FRIEDMAN. And with simple expectant therapy.

DR CARROLL S. WRIGHT. Dr J. W. Lentz treated a patient with penicillin administered intramuscularly, resulting in a very rapid recovery.

DR LOUIS GOLDSTEIN. The patient used bismuth-formic iodide compound powder. Is it possible that this man is sensitive to iodine and that this disease is an iododerma?

DR CARROLL S. WRIGHT. That is a great deal of destruction for iodine.

DR J. P. GUEQUIERRE. I have seen similar effects from saponated solution of cresol.

#### **Pemphigus Vulgaris, Improved by Acetarsone** Presented by DR CARROLL S. WRIGHT and DR MEYER L. NIEDELMAN

E. G., a white woman aged 51, felt pain and soreness in the mouth two years ago. Small painful blebs formed on the buccal mucous membrane. Shortly thereafter, the tongue became involved. There also developed small blebs on the larynx and posterior pharyngeal wall and a few lesions in the nares. About one month previous to her visit to the clinic, crops of bullae appeared on the back, chest and arms. There was no history of ingestion of drugs or iodized salt.

The patient's general appearance is only fair, with a certain degree of emaciation, as she has lost 10 pounds (4.5 Kg) within a period of three months. She presents erosive lesions on the posterior part of the pharynx, mouth and tongue. Her back, chest and arms are covered with large bullae and blebs.

Biopsy from a lesion on the back confirmed the diagnosis of pemphigus vulgaris.

A urinalysis was normal. The blood count was normal except for a leukocytosis of 15,000. The blood glucose value was 78 mg and the Wassermann reaction of the blood was negative.

Treatment consisted of use of acetarsone tablets (0.25 Gm), according to the following schedule: 1 tablet dissolved in a small amount of water each morning for three mornings on an empty stomach, the following week, 2 tablets each morning for three mornings, and

the third week, 2 tablets the first morning and 3 tablets the following two mornings. The patient was kept on the last schedule until she had taken as many tablets as there were kilograms of body weight. The dose of the tablets was then reduced, and the interval increased. She has taken to date 120 tablets with no ill effects. She also received vitamin B complex, a bland diet and 5 per cent boric acid ointment applied locally. At present she has no lesions and has gained weight.

#### DISCUSSION

DR D. M. SIDLICK. The diagnosis is obvious, but it prompts the question: What is pemphigus? In March 1943, I presented before the Atlantic Dermatologic Conference a child aged 4 years, and one dermatologist stated that he could not accept the diagnosis of pemphigus because the child was alive! If that is the criterion then perhaps this child will conform to it, for she is losing ground rapidly.

DR CARROLL S. WRIGHT. All of us see patients who have these lesions, but for some we are able to make a diagnosis only after they die. Many dermatologists saw this patient, and all made the diagnosis of pemphigus.

DR D. M. SIDLICK. I know a patient for whom a diagnosis of pemphigus was made by more than one dermatologist and who was on the verge of dying. He recovered and remained well for seven years, but now the disease has relapsed into its original state.

#### **Mycosis Fungoides Exhibiting Large Concentric Lesions and Treated with Testosterone** Presented by DR JOHN F. WILSON

F. B., a merchant seaman aged 49, recently returned from India, presents red dry, scaly and eczematoid lesions of the face, some of which are infiltrated. On the right side of the chest is an elevated lesion 3 cm in diameter with a red granulating surface. There are numerous dry, scaly lesions on other parts of the body. These lesions are of circular outline with clearing in the center. The back of the right knee shows a red oozing area, the site of a previous tumor-like lesion. The patient has had an itching eruption since January 1943. He was treated at another hospital in August 1943, and a diagnosis of premycotic mycosis fungoides was made. He was admitted to yet another hospital on Dec 3, 1943. At that time he presented a dry, scaly, excoriated eruption of the face, trunk and legs. Several of the lesions on the back were infiltrated heavily and elevated. There were large tumor lesions of the left temporal region and left popliteal region. A few days later he was admitted to another hospital for disease of the gallbladder. A diagnosis of mycosis fungoides was made, and he was treated with roentgen rays. In January 1944 he was readmitted to the same hospital, for treatment of lobar pneumonia. He returned to the original hospital at the end of January 1944, and, although there was some improvement, he had lost 25 pounds (11.3 Kg) in weight and appeared ill and his skin was still eczematous, with many infiltrated areas and remnants of tumor-like lesions.

The mucous membranes are pale. The left epitrochlear and right inguinal lymph nodes are enlarged.

A complete blood count revealed 11 Gm of hemoglobin, 3,520,000 erythrocytes and 9,400 leukocytes, with 76 per cent polymorphonuclear leukocytes, 20 per cent lymphocytes and 4 per cent eosinophils. Chemical examination of the blood showed 69 mg of total protein (36 mg of albumin and 33 mg of globulin) and 63 mg of sugar per hundred cubic centimeters. The blood

urea nitrogen level was 12 mg and the blood cholesterol level 245 mg. A urinalysis resulted in normal values.

The patient has been given testosterone propionate, 25 mg intramuscularly once weekly and 10 mg orally daily since March 24, 1944, with resultant general improvement and a gain in weight of 30 pounds (13.6 Kg.)

#### DISCUSSION

DR LOUIS GOLDSTEIN: What was the reason for the treatment with testosterone?

DR JOHN F. WILSON: Recently Drs. Gerb and Wise (*ARCH. DERMAT. & SYPH.* 48:359-368 [Oct.] 1943) reported that they treated a patient with mycosis fungoides with bullous lesions with testosterone.

DR FRED D. WEIDMAN: I was struck by the fact that the patient did not have any lymphadenopathy tonight. This is a highly infiltrated granuloma fun-

goides. In view of that fact and the concentric lesions which resemble those of *tinea imbricata*, I think that a biopsy should be made.

DR JOHN F. WILSON: This man came to the Philadelphia General Hospital on December 3 with typical tumor lesions of mycosis fungoides. Two days later, before a biopsy was performed, he had an acute attack of disease of the gallbladder and was sent to another hospital, where a diagnosis of mycosis fungoides was made on clinical grounds. He was given a certain amount of roentgen ray treatment at that time. When he was seen again, the tumors had almost entirely disappeared. He did not have the concentric lesions then nor did he have them when I first saw him, in December.

DR FRED D. WEIDMAN: I personally have never seen such concentric lesions on patients with mycosis fungoides, nor have I seen them in illustrations.

NOTE.—A biopsy was performed, and the diagnosis of mycosis fungoides was substantiated.

## Book Reviews

**On Modern Syphilotherapy with Particular Reference to Salvarsan** By Albert Neisser, M D  
Translated by Isabelle von Sazenhofen Wartenberg  
Biography and Bibliography by Frances Tomlinson  
Gardner Price, \$1 Pp 42 Baltimore Johns  
Hopkins Press, 1945

In the brief space of forty-two pages Wartenberg and Gardner have brought together a condensed translation into English of one of Neisser's most important contributions to syphilotherapy. A biography and a bibliography of Neisser's works are included. This material appeared in the *Bulletin of the History of Medicine* (16 469-510 [Dec] 1944).

The biographic sketch is rightly placed first and is excellently written in trenchant English. It avoids ponderosity, dwells on the highlights of Neisser's life and holds the reader's interest to the end. Neisser, however, was such an Olympian and accomplished so much in medicine that this reviewer found the sketch too brief. On page 2, third line from the top, the author states that "skin diseases were only dimly understood in the last half of the nineteenth century." This statement is entirely controverted by the fact that in the space of time mentioned (1850 to 1900) dermatology was an active specialty, as is evidenced by the publication of some eighteen or more textbooks in English and approximately the same number in French and German. The French *Annales des maladies de la peau* appeared in 1843, the British *Journal of Cutaneous Medicine and Diseases of the Skin*, in 1867, and the *American Journal of Syphilography and Dermatology*, in 1870.

Between 1850 and 1880 France, England and Germany were famous centers of dermatologic teaching. In 1869 the New York Dermatological Society was founded and in 1876 the American Dermatological Association. In 1871 Harvard University founded a professorial chair

in dermatology. Certainly such progress and activity in dermatology could not exist between 1850 and 1900 if diseases of the skin were only "dimly understood."

On page 3, fifteenth line from the bottom, there is a misprint, Hansen's name is spelled "Hanson."

The English translation of Neisser's "Ueber moderne Syphilistherapie mit besonderer Berücksichtigung des Salvarsans," though first published in German thirty-four years ago, can be read with profit by the syphilologist of today.

The bibliography of a man as important as Albert Neisser is always of great help, and its addition to the monograph should prove most welcome. It is a monument to his genius.

**Outline of the Amino Acids and Proteins** Edited by Melville Sahyun, M A, Ph D Price, \$4 Pp 236 New York Reinhold Publishing Corporation, 1945

Over a dozen contributing authors present this symposium on amino acids and proteins. It is needless to recall that for the biologic sciences knowledge of the proteins and of their amino acid building stones is fundamental. As for medical science, it is in the midst of an era marked by an acute awareness of the nutritional factors in disease processes.

This book offers the physician a concise, simply presented account of the more or less accepted facts in the fascinating story about amino acids and proteins. The presentation deliberately avoids the technical and abstruse, and thus the book is substance easy to digest for the physician.

The reviewer recommends this book highly to the dermatologist who accepts the necessity for continual sustenance in the basic sciences.

## CARBOHYDRATE METABOLISM AND THE SKIN

ERICH URBACH, M.D., AND JOHN W. LENTZ, M.D.  
PHILADELPHIA

For many years one of us (E. U.)<sup>1</sup> has pointed to the fact that in the study of the physiology and pathology of the skin a chemical analysis of the skin excised from the living organism gives a far better insight into the metabolic processes of that organ than does a study of the blood alone. With regard specifically to the carbohydrate metabolism of the skin, the blood sugar tolerance test, which is generally so dependable, has been found unreliable in a number of instances.<sup>2</sup> Urbach<sup>3</sup> has introduced the electric punch biopsy method, with which skin can be removed almost painlessly, without anesthetics of any kind, even when the procedure is performed repeatedly for a series of studies. At the same time, microchemical methods have been perfected which make it possible to carry out an accurate determination of sugar in minute tissue particles. This method has been used to determine the free<sup>4</sup> and bound<sup>5</sup> sugar in the normal skin of man and animals and also to study the carbohydrate metabolism of the skin under pathologic conditions and in a variety of cutaneous diseases.

Since some of these investigations were originally carried out in Vienna, on persons whose diet was much higher in carbohydrate and fat

than the usual American diet is, we decided that we might profitably repeat these studies here with a larger experimental material. For this purpose 60 biopsy specimens were obtained in duplicate from 36 patients with various diseases of the skin and 10 persons, used as controls, who were free from cutaneous manifestations and from diabetes. In addition, the results of a previous similar study<sup>1</sup> carried out on 90 patients are incorporated in this report.

The 36 patients who were more recently studied consisted of 11 with eczema of various causation, 7 with psoriasis, 6 each with staphylococcal infection and mycotic infection, 2 each with pruritus and xanthoma tuberosum and 1 each with rosacea and epithelioma of the face. Three of the 36 patients had diabetes mellitus, added to 9 previously reported diabetic patients makes this a total of 12 (table 8).

In 7 cases determinations of the sugar in the blood and in the skin were repeated three times within five to six weeks. The first time the patients were on their usual diets, the second time as nearly as possible on a carbohydrate-free diet, and lastly on a regimen very low in fat. In the last instance, 3 patients were also restricted in their consumption of carbohydrates.

Lastly, the relative proportions of skin sugar to blood sugar were studied in six different species of animals.

## BIOPSY PROCEDURE

Two specimens of skin are excised by means of a rapidly rotating, motor-driven punch, 5 mm in diameter. The punches are inserted into the shaft of a small motor<sup>6</sup> of the kind ordinarily used in hand drills. With this device, uniform pieces of skin can be removed within a few seconds. The pieces are snipped off at the base with the scissors. The wound is then briefly swabbed with a 2 per cent aqueous solution of gentian violet medicinal followed by thymol iodide powder for disinfection purposes. When the operation is performed rapidly, the excised piece of skin is free of blood. Great care must be taken to remove the subcutaneous fat.

6 Hand—EE # 13 aAB, manufactured by the Chicago Wheel and Mfg Co., 1101 W. Monroe Street, Chicago. Punches manufactured by Jerome Ward, 1315 McKinley Street, Philadelphia.

Expenses for this work were defrayed in part by a grant from the Allergy Research Foundation, Inc., Philadelphia.

From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine, Dr. John H. Stokes, Director.

1 Urbach E, Die biologisch-chemische Forschungsrichtung in der Dermatologie, Wien klin Wchnschr 41 581, 1928.

2 Urbach E, Depisch F, and Sicher G. Zum Problem des isolierten hohen Hautzuckers bzw Hautdiabetes, Klin Wchnschr 16 452, 1937.

3 Urbach E, and Fantl E. Methoden zur quantitativ-chemischen Analyse der Haut I Allgemeine Prinzipien, Biochem Ztschr 196 471, 1928.

4 Urbach E, and Sicher G. Der Zuckergehalt der Haut unter physiologischen und pathologischen Bedingungen, Arch f Dermat u Syph 157 160, 1929.

5 Urbach E, and Rejtoe K. Ueber den freien und "gebundenen" Zucker in der Haut unter physiologischen, experimentell veraenderten und pathologischen Bedingungen bei Mensch und Tier, Arch f Dermat u Syph 166 478, 1932.

from the biopsy specimens, and with some experience this is easy enough to do when dealing with human skin, for the yellowish fat can readily be distinguished from the white tissue of the cutis. Dog's skin presents greater difficulties in this respect, for the fat which is closely interwoven with the lower layers of the cutis has the same whitish color as the cutis. In order to obtain corresponding values in both specimens, it is necessary to remove the subcutaneous fat up to the dark upper layer of the cutis, studded with hair follicles.

For the purpose of uniformity the specimens of skin are usually taken from the upper third of the exterior aspect of the thigh because the various areas of skin present appreciable differences so far as their water content is concerned (Nadel<sup>7</sup>). This, of course, has an influence on the sugar content. The specimens of skin usually weigh from 30 to 40 mg, but they may weigh between 20 and 50 mg, depending on their texture, on the skin's state of nourishment and on the age and race of the patient.

In our work with dogs we always put the animals to sleep in order to obviate an increase in blood sugar due to emotional disturbance such as fear or struggle against bonds. The narcotic used was chloralose, of which 0.1 Gm per kilogram of body weight in a 10 per cent solution in 10 per cent alcohol was administered intravenously. Anesthesia sets in immediately and lasts about four hours. The animals must be kept well covered for the duration of the experiment, otherwise they may suffer fatal chills. Preliminary experiments have convincingly demonstrated that the sugar level in the blood and the skin was not appreciably influenced by chloralose narcosis.

In our earlier experiments we employed the microchemical method suggested by Urbach and Fantl,<sup>8</sup> which was based on the principle of the Hagedorn-Jensen method. Pillsbury and Kulchar<sup>9</sup> checked this procedure in experiments on amyotized rabbits and guinea pigs and obtained similar reliable figures for skin sugar. It was subsequently discovered, however, that the values originally given for free sugar were too low, because a part of the sugar in the tissues had escaped chemical detection as a result of the presence of considerable quantities of amino acid nitrogen in the skin.<sup>5</sup> We eliminated this error by employing Rappaport's<sup>10</sup> method, which achieves precipitation in an alkaline medium. The values determined by means of the improved

method were found to be about 20 per cent higher in human beings than the previously reported figures.

An advantage offered by this method is that it enables the investigator to determine the precise sugar content of biopsy specimens weighing no more than 20 to 30 mg. This, in turn, permits the use of smaller pieces of skin than formerly, which obviates the necessity of suturing the wounds.

Since it is somewhat difficult to obtain a description of Rappaport's procedure, we shall describe it here in detail.

#### CHEMICAL PROCEDURE

**Principle.** Heated potassium ferricyanide is reduced by sugar, and the excess of ferricyanide is iodometrically determined.

**Reagents for Dealbumination**

(1) 0.45 per cent zinc sulfate solution made from a 45 per cent stock solution.

(2) Fiftieth-normal sodium hydroxide.

**Reagents for Sugar Determination**

(3) A potassium ferricyanide and phosphate buffer solution made (a) by dissolving 0.9 Gm of ferricyanide in water and diluting to 1 liter in a measuring flask, and (b) by dissolving 210 Gm of potassium dihydrogen phosphate and 63.75 Gm of potassium orthophosphate in water and diluting to 1 liter. The ferricyanide solution and the phosphate buffer should be mixed in equal parts before using.

(4) Zinc sulfate-potassium iodide. To 20 per cent zinc sulfate solution (prepared from pure zinc sulfate dissolved in distilled water) add just before using enough solid potassium iodide to form a 2.5 per cent potassium iodide solution. This reagent should be prepared freshly every day.

(5) 20 per cent phosphoric acid. Dilute 20 cc of syrupy phosphoric acid with water to make 100 cc of solution.

(6) Thousandth normal sodium thiosulfate. To 10 cc of tenth-normal sodium thiosulfate add 12 cc of normal sodium hydroxide in a 1,000 cc flask and dilute to the mark.

(7) 0.25 per cent starch solution.

**Procedure for Venous Blood.** For each weighing glass (65 by 16 mm) use three control glasses. Fill each glass with 1 cc of sodium hydroxide (reagent 2). Take up 0.02 cc of blood with an exactly calibrated capillary pipet. Carefully clean the pipet of any blood adhering to the outside and blow the contents into the sodium hydroxide solution. Clean the pipet by taking up and blowing out the sodium hydroxide three times.

Then add 1 cc of zinc sulfate (reagent 1) and put the glasses into boiling water for three minutes. Cool to room temperature and filter through small funnels (diameter of upper edge 25 to 30 mm, stem thinned out near the top end), which contain a small roll of absorbent cotton washed with hot water, into Hagedorn-Jensen test tubes.

Wash the glasses three times with 1 cc of hot water and pour the wash water onto the filter. Let the liquid drain thoroughly, then press the cotton with a fine glass rod. Pipet into the test tubes 2 cc of the ferricyanide-phosphate mixture (reagent 3).

<sup>7</sup> Nadel, A. *Chemische Studien an der menschlichen Haut*, Arch f Dermat u Syph **166** 507, 1932.

<sup>8</sup> Urbach, E., and Fantl, E. *Methoden zur quantitativ-chemischen Analyse der Haut*, Biochem Ztschr **196** 474, 1928.

<sup>9</sup> Pillsbury, D. M., and Kulchar, G. V. *The Use of the Hagedorn-Jensen Method in the Determination of Skin Glucose*, J Biol Chem **106** 351, 1934.

<sup>10</sup> Rappaport, F. *Mikrochemie des Blutes*, Vienna, Emil Haim & Co., 1936.



Put the tubes into a boiling water bath for twenty minutes for reduction. After cooling, add 1 cc of zinc sulfate-potassium iodide solution (reagent 4) and 1 cc of phosphoric acid solution (reagent 5). Titrate with thousandth normal sodium thiosulfate (reagent 6) from microburet after adding a few drops of starch solution (reagent 7) until colorless. The change in color is pronounced in spite of the dilute sodium thiosulfate solution.

#### Calculation

(Sodium thiosulfate used for control minus sodium thiosulfate used for blood)  $\times$  174 equals sugar content in milligrams per hundred grams.

**Changes to be Made for Use on Cutaneous Tissue**  
The weight of a weighing glass with 1 cc of zinc sulfate solution is determined and a small piece of skin added and the glass weighed again. One cubic centimeter of fiftieth-normal sodium hydroxide is used to wash off the scissors and the forceps used for cutting the skin. Zinc sulfate should be added, before the sodium hydroxide when one works with tissue, because the skin swells in the sodium hydroxide and makes it impossible to dissolve out all the sugar.

In order to avoid taking numerous biopsy specimens in the course of lengthy investigations, a number of authors chose to examine dextrose content of blisters induced by cantharides. However, on the basis of painstaking studies<sup>11</sup> we have demonstrated that the fluid from blisters produced by cantharides can definitely not be regarded as chemically representative of cutaneous tissue and cannot, therefore, serve as a substitute for biopsy specimens for chemical investigations.

#### SUGAR CONTENT OF THE SKIN UNDER PHYSIOLOGIC CONDITIONS IN MAN AND ANIMALS

**Free Sugar in the Skin** Studies on the fasting subjects living under similar dietary conditions reveal that the skin of man and animals presents a relatively constant sugar level. Thus determinations of the fasting skin sugar repeated after eight to ten weeks on several persons on the same diet have shown differences of only 2 to 3 per cent. However, the skin sugar level varies from species to species. Table 1 shows that man has the lowest absolute skin sugar value, an average of 58 mg per hundred grams. The mean blood sugar level is 94 mg per hundred cubic centimeters. The proportion of skin sugar to blood sugar is about 61.4 per cent. The sugar content of the skin and its relation to the blood sugar are in no way dependent on the age of the person. On the other hand, as we shall presently demonstrate, dietary habits exert a decided influence in this respect. In this connection

it is interesting to note that in Vienna the average values were as follows: blood sugar 103 per hundred cubic centimeters, skin sugar 61 per hundred grams. These figures are definitely higher than those arrived at for our Philadelphia material. This, we feel, may unquestionably be explained by the fact that the usual diet in Austria was appreciably higher in carbohydrates. In animals, with the exception of the mouse, the sugar content of the skin is higher than that of the blood. The highest values for skin sugar are found in guinea pigs and cats.

**Bound Sugar in the Skin** Determination of the rate of the so-called free sugar does not mean that the entire carbohydrate content of the skin has been accounted for. As early as 1855 Fignier observed that the reducing capacity of the blood showed a decided increase after the blood has been boiled with an acid. These reducing substances have generally been termed bound sugar. Bierly coined the term *sucric proteidique* (protein sugar). Whereas free sugar

TABLE 1—Level of Free Sugar of Blood and Skin in Man and in Animals

| Subject    | Mg Sugar per 100 Cc Blood | Mg Sugar per 100 Gm Skin | Blood/Skin Sugar Ratio, per Cent |
|------------|---------------------------|--------------------------|----------------------------------|
| Man        | 94                        | 58                       | 61                               |
| Mouse      | 114                       | 77                       | 67                               |
| Dog        | 81                        | 87                       | 103                              |
| Rat        | 85                        | 106                      | 125                              |
| Rabbit     | 105                       | 134                      | 128                              |
| Guinea pig | 110                       | 145                      | 132                              |
| Cat        | 97                        | 148                      | 151                              |

is composed mainly of glucose, bound sugar, on the other hand, is composed chiefly of mannose and glucosamine. In a previously published paper,<sup>5</sup> we specifically have pointed out that, in addition to the free sugar, the bound sugar contains certain reducing substances which are released by hydrolysis. Therefore, in full agreement with Grevenstuck<sup>12</sup> we should like to stress here that when we employ the term bound sugar we are well aware of the fact that this term is not strictly accurate. To be absolutely correct and specific, we should have to say, at some length, that we are dealing here with a number of substances whose capacity for reducing is increased by hydrolysis with acids.

Urbach and associates<sup>7</sup> have determined the quantity of bound sugar in the skin of man and animals. In the former, it is about fifteen times greater than the value for free sugar in the skin, and one and one-half times that of the

<sup>11</sup> Urbach, E. Ueber den prinzipiellen Unterschied in der chemischen Zusammensetzung von Hautblaseninhalten und intravital entnommenem Hautgewebe, *Klin Wchnschr* 8 2094, 1929.

<sup>12</sup> Grevenstuck, A. Ueber freien und "gebundenen" Zucker in Blut und Organen, *Ergebn d Physiol* 28.1, 1929.

bound sugar in the blood In animals, the skin also contains far more bound sugar than free sugar, although the preponderance is not as great here as it is in man This proportional difference is due, in part, to the fact that the free sugar concentration is higher in the skin of animals than in the human skin (table 2) When rabbits are kept on different kinds of diets (green fodder, high carbohydrate diet, mixed

TABLE 2—Bound Sugar in the Blood and Skin of Man and Various Animals

| Subject    | Total Sugar after Acid Hydrolysis (Bound Sugar) |                       | Ratio of Skin Sugar to Blood Sugar, per Cent |
|------------|---|-----------------------|--|
|            | Mg per 100 Cc in Blood                          | Mg per 100 Gm in Skin |  |
| Man        | 543   | 884                   | 163  |
| Dog        | 608   | 1,082                 | 178  |
| Rabbit     | 495   | 885                   | 178  |
| Guinea pig | 428   | 776                   | 181  |

diet) we find that the animals that have been fed large quantities of carbohydrate show considerable greater amounts of bound sugar in the skin than do those that have been kept on a green fodder diet

In diabetic human beings and in dogs with experimentally induced diabetes the bound sugar level of the skin is considerably above the normal (table 3) In terms of total bound sugar the skin is surpassed only by muscle tissue due to the great quantitative preponderance of the latter in the body

On the other hand, there is no demonstrable connection between dermatoses and the bound sugar concentration of the blood, not even when large amounts of sugar are ingested

TABLE 3—Free and Bound Sugar Content of Various Tissues of Pancreatectomized Dog

|                                  | Free Sugar | Bound Sugar |
|----------------------------------|------------|-------------|
| Blood (mg per 100 cc)            | 320        | 1,068       |
| Skin (mg per 100 Gm)             | 256        | 2,329       |
| Subcutaneous fat (mg per 100 Gm) | 78         | 542         |
| Muscle (mg per 100 Gm)           | 227        | 2,276       |
| Liver (mg per 100 Gm)            | 821        | 2,185       |

\* Examined one week after pancreatectomy

SKIN SUGAR TOLERANCE TEST

We have also studied the reaction of the skin sugar level to the sugar tolerance test We<sup>13</sup> prefer the oral to the intravenous method because the former, which comes closer to reproducing the conditions of carbohydrate ingestion, constitutes the better functional test of the pancreas

13 Urbach, E Perorale oder intravenoese Zuckerbelastung zur Pruefung der glykaemischen Reaction? Klin Wchnschr 11 1789, 1932

When glucose (100 Gm) is given by mouth, the maximal level in the blood is reached within half an hour, while the maximal concentration in the skin is not observed before an hour after administration

In those cases in which the blood sugar returns to its original level within two hours it takes the skin sugar curve three hours to drop to its starting point, and thus takes even an

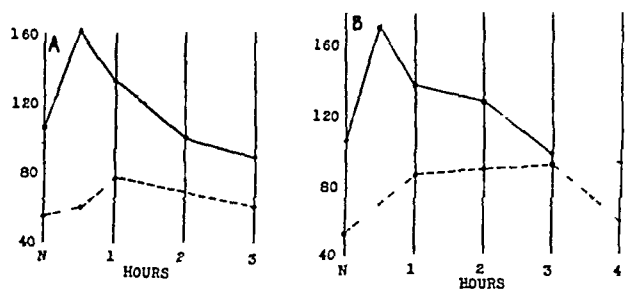


Fig 1—Normal sugar tolerance curves of the blood and the skin in man The unbroken line indicates blood sugar, the broken line skin sugar in all the charts

hour longer in those not uncommon cases in which it takes the blood itself three hours to register a decline in the hyperglycemia (fig 1)

SUGAR CONTENT OF THE SKIN UNDER VARIOUS DIETARY CONDITIONS

The opinion is still widely held that the diet has little, if any, influence on the fasting blood sugar level in man and animals This does not by any means hold true in all cases In an extensive series of experiments on human subjects we were able to ascertain that the fasting rates

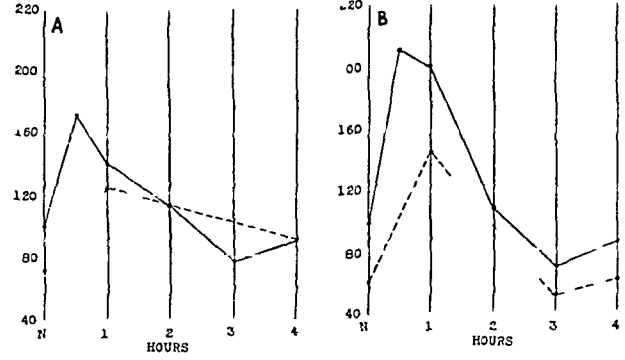


Fig 2—Influence of a low carbohydrate diet on the blood sugar curve A, curves when the subject was on the usual diet, B, after a diet low in carbohydrates and high in protein

in both the blood and the skin are directly influenced by the carbohydrate content of the diet

Even more clearly evident is the influence exerted by the diet on the behavior of the blood sugar curve following administration of massive quantities of sugar Thus figure 2 B shows the response of a patient who had been maintained on a carbohydrate-free diet, a blood sugar of

210 was found thirty minutes after ingestion of 100 Gm of sugar. On the other hand, when the patient was fed a mixed diet, a level of only 170 was noted, following the glucose meal (fig 2A). This difference in response can be demonstrated even more strikingly in experiments on animals. For example, when a dog on a diet entirely free from carbohydrates was given sugar, 15 Gm per kilogram of body weight (fig 3B), the blood sugar rose to 280, as compared with 134 when the animal was kept on a strict carbohydrate diet (fig 3A). Similar findings have been reported by Himsworth<sup>14</sup>

man (fig 2B) and animals (fig 3B) on a low carbohydrate diet than in subjects that have been on a mixed or a high carbohydrate diet. Moreover, the skin sugar curve like the blood sugar curve rises steeply one hour after administration of sugar and then returns rapidly to normal or even subnormal levels (figs 2B and 3B). These pathologic curves may serve as a warning against carrying out glucose tolerance tests when the patient is on a low sugar diet.

Toshima<sup>16</sup> kept rabbits on a diet extremely rich in sugar for three months and noted, in agreement with our findings, that the fasting

TABLE 4—Influence of Low Carbohydrate Diet on the Fasting Sugar Content of Blood and Skin

| Patient | Age | Sex | Disease         | After Normal Diet |                |       | After Low Carbohydrate Diet (3 Weeks) |                |       |
|---------|-----|-----|-----------------|-------------------|----------------|-------|---------------------------------------|----------------|-------|
|         |     |     |                 | Blood Sugar, Mg   | Skin Sugar, Mg | Ratio | Blood Sugar, Mg                       | Skin Sugar, Mg | Ratio |
| M W     | 45  | F   | Psoriasis       | 104.2             | 63.4           | 60.8  | 90.3                                  | 55             | 60.9  |
| H B     | 44  | M   | Furunculosis    | 113               | 69.4           | 61.4  | 86.8                                  | 53.5           | 61.9  |
| A W     | 38  | M   | Dermatophytosis | 113.2             | 68.1           | 60.1  | 93.2                                  | 57.5           | 62.0  |
| S B     | 30  | M   | Xanthoma        | 111.2             | 61.4           | 59.3  | 97.1                                  | 59.8           | 61.6  |
| W M     | 70  | M   | Epithelioma     | 105               | 63.5           | 60    | 86.9                                  | 53.7           | 61.7  |

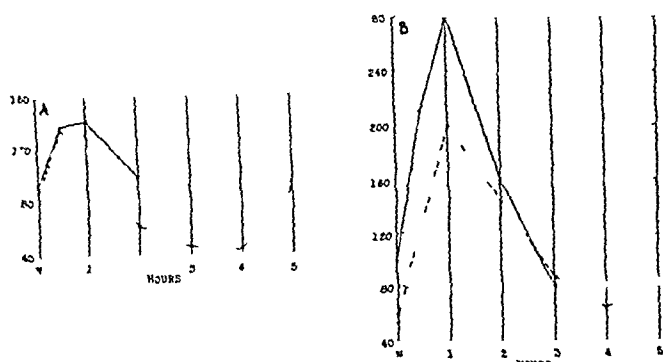


Fig 3—Influence of various diets on the sugar tolerance curves of blood and skin in the same dog. A, curves after a dog had received a pure carbohydrate diet for a week; B, after it had received a pure meat diet for a week.

In our opinion, this sugar curve is not, as Uchida<sup>15</sup> and other authors claim, similar to a diabetic response, we feel that it is to be interpreted as a glycemic reaction of the sympathetic type (see following text). Our views are based on the facts that (1) the peak of the reaction is speedily reached, (2) the level soon returns to normal, and, above all, (3) the curve shows an ensuing hypoglycemia.

The skin responds in a similar manner. The fasting skin sugar level is definitely lower in

blood and skin sugar levels were definitely higher than in animals on a normal diet.

Tsukada's<sup>17</sup> experiments are especially interesting. They demonstrate that while the skin sugar level is largely dependent on the acid or alkaline character of the diet, the blood sugar is more or less independent of the acidity of the food. For example, in animals fed on oats or cabbage the skin sugar tolerance shows appreciable fluctuations, while the blood sugar remains virtually constant in almost all cases. The skin sugar tolerance is increased by an acid ash diet (oats) and decreased by alkaline ash food (cabbage). Similarly, hydrochloric acid and sodium bicarbonate, administered by mouth, exert an influence on the skin's capacity to absorb sugar, the former increasing and the latter decreasing this capacity.

Thus, Tsukada's investigations disclose the highly significant fact that not only the carbohydrate content of the diet, but also its acid and base constituents exert a definite influence on both the sugar level and the sugar tolerance of the skin. Further studies carried out by this author would seem to warrant the assumption that other contributing factors, such as the auto-

<sup>14</sup> Himsworth, H. P. Mechanism of Diabetes Mellitus, Lancet 2 1, 1939.

<sup>15</sup> Uchida, K. Untersuchungen ueber den Einfluss von Traubenzucker und Dioxyceton auf den Blutzuckerspiegel unter wechselnden Bedingungen, Biochem Ztschr 194 111, 1928.

<sup>16</sup> Toshima, E. Hautzucker bei Zuckerstoff-Ueberfuetterung, Jap J Dermat & Urol 36.405, 1934.

<sup>17</sup> Tsukada, S. Experimentelle Untersuchungen ueber die Schwankung des Haut- und Blutzucker-gehaltes unter verschiedenen Bedingungen, Tohoku J Exper Med 21 347, 1933.

onomic nervous system and the ductless glands, may exert an influence on the skin's capacity to absorb and to release sugar, often independently of the blood sugar

As mentioned before, Urbach and Rejtoe <sup>5</sup> have shown that animals on a high carbohydrate diet possess considerably greater quantities of bound sugar in the skin than do those animals that have been kept on a normal diet

Especially interesting is the question as to the influence which either a high fat or low fat diet may have on the carbohydrates of the blood and of the tissues With regard to a diet high in fat, Adlersberg and Porges <sup>18</sup> have pointed out that in diabetic persons this kind of diet seriously disturbs the capacity to assimilate carbohydrates and greatly lowers the sugar tolerance Stolte, <sup>19</sup> as well as Hirsch-Kauffmann and Knauer <sup>20</sup> have demonstrated that a high fat intake creates a frank hyperglycemia in diabetic and nondiabetic persons alike According to Himsworth <sup>21</sup> both men and animals kept on a diet high in fat present more prolonged and far more pronounced hyperglycemia following administration of glucose than do subjects on a diet high in carbohydrates

In experiments on rabbits, Sikinami and Hosokawa <sup>22</sup> claimed that administration of fat, in the form of 2 cc of cod liver oil, resulted in a greater increase in the sugar content of the skin than in that of the blood They obtained the same response from a single administration as from repeated doses of cod liver oil However investigations carried out by ourselves <sup>22a</sup> gave rather different results as far as the influence of fat intake on skin sugar is concerned As can be seen from table 5, the administration of 2 cc of cod liver oil to fasting rabbits previously on a normal diet produced a progressive decrease in the skin sugar amounting to more than 10 per cent after three hours, while at the same

time the blood sugar showed a slight tendency to increase

This trend was even more pronounced when animals were fed 2 cc cod liver oil daily for one week (table 6) The fasting skin sugar of rabbits so prepared shows a drop of about 23 per cent while the blood sugar is practically unchanged

The explanation of the difference between our observations and those of Sikinami and Hosokawa is in all probability a faulty method used by the Japanese authors in determining skin sugar It is sufficient to state that their skin sugar levels are far below the blood sugar levels

TABLE 5—Influence of Single Administration of Fat on the Blood Sugar and Skin Sugar of Normal Rabbits

|                                      | Rabbit 1        |                |       | Rabbit 2        |                |       |
|--------------------------------------|-----------------|----------------|-------|-----------------|----------------|-------|
|                                      | Blood Sugar, Mg | Skin Sugar, Mg | Ratio | Blood Sugar, Mg | Skin Sugar, Mg | Ratio |
| Fasting                              | 104             | 134            | 129   | 106             | 136            | 128   |
| One hour after 2 cc cod liver oil    | 106             | 130            | 123   | 108             | 130            | 120   |
| Two hours after 2 cc cod liver oil   | 108             | 124            | 115   | 110             | 126            | 115   |
| Three hours after 2 cc cod liver oil | 112             | 120            | 107   | 108             | 122            | 113   |

TABLE 6—Influence of Repeated Administration of Fat on the Fasting Blood Sugar and Skin Sugar of Normal Rabbits

|  | Rabbit 3                |                        |       | Rabbit 4                |                        |       |
|--|-------------------------|------------------------|-------|-------------------------|------------------------|-------|
|  | Fasting Blood Sugar, Mg | Fasting Skin Sugar, Mg | Ratio | Fasting Blood Sugar, Mg | Fasting Skin Sugar, Mg | Ratio |
| On normal diet   | 100                     | 134                    | 134   | 107                     | 188                    | 129   |
| On normal diet + 2 cc cod liver oil daily for ten days | 93                      | 102                    | 107   | 105                     | 107                    | 102   |

Finally we studied the influence of a low fat diet on the fasting blood sugar and skin sugar in man Persons who adhered to the low fat regimen for five weeks showed a definitely higher blood sugar and skin sugar than when they were maintained on a low carbohydrate intake (table 7)

SUGAR CONTENT OF THE SKIN UNDER PATHOLOGIC CONDITIONS IN MAN AND IN ANIMALS

In diabetes mellitus the ratio between skin sugar and blood sugar shifts in favor of the skin Thus we observed 7 diabetic patients who presented an average fasting blood sugar level

18 Adlersberg, P, and Porges, O *Fettnahrung und Kohlehydrattoleranz*, Med Klin **27** 1783, 1931  
19 Stolte, K *Freie Diet beim Diabetes (Erwiderungen auf die Ausfuehrungen des H Prof Carl v Noorden)*, Med Klin **29** 288, 1933  
20 Hirsch-Kauffmann, H, and Knauer, H *Ueber den Einfluss von Kohlehydrat- und Fettzufuhr auf Glykaemie und Lipidstoffwechsel*, Med Klin **29** 562, 1933  
21 Himsworth, H P *Influence of Diet on Sugar Tolerance of Healthy Men and Its Reference to Certain Extrinsic Factors*, Clin Sc **1** 251, 1934  
22 Sikinami, Y, and Hosokawa, H *Ueber die Hautzuckererhoehung und die Leberglykogenverminderung nach Fettbelastung*, Tohoku J Exper Med **35** 257, 1939  
22a Urbach, E, and Lentz, J W *Influence of High Fat Diet on the Skin Sugar in Rabbits* J Invest Dermat to be published

of 155 mg per hundred cubic centimeters and a skin sugar level of 103 mg per hundred grams a ration of 66.4 per cent

The diabetic skin sugar curve in man (fig 4A) shows certain typical peculiarities during the tolerance test. The peak of the rise in diabetic patients is generally not reached in the blood until two hours have passed, and not until well toward the end of the third hour as far as the skin is concerned. Accordingly the skin sugar level is still high after four hours,

administration of glucose, is just as dependent on the pancreas as the blood sugar curve has long been known to be.

Turning to cases of mild diabetes in man, it is necessary as far as fasting skin sugar levels are concerned to distinguish between two categories, namely those with and those without manifestations in the skin. In the former we include notably such manifestations as recurrent furunculosis, hidrosadenitis axillaris, eczema, urticaria and pruritus among cutaneous diseases of sig-

TABLE 7—Difference in Effect Between Low Fat and Low Carbohydrate Diets on Fasting Sugar of Blood and Skin

| Patient | Age | Sex | Disease     | After Normal Diet |                |       | After Low Carbohydrate Diet |                |       | After Low Fat Diet |                |       |
|---------|-----|-----|-------------|-------------------|----------------|-------|-----------------------------|----------------|-------|--------------------|----------------|-------|
|         |     |     |             | Blood Sugar, Mg   | Skin Sugar, Mg | Ratio | Blood Sugar, Mg             | Skin Sugar, Mg | Ratio | Blood Sugar, Mg    | Skin Sugar, Mg | Ratio |
| W. M.   | 70  | ♂   | Epithelioma | 105               | 63.5           | 60    | 86.9                        | 53.7           | 61.7  | 103.5              | 64.2           | 62    |
| M. W.   | 45  | ♀   | Psoriasis   | 104.2             | 63.4           | 60.8  | 90.3                        | 55.0           | 60.9  | 105                | 67.2           | 62.2  |
| R. B.   | 30  | ♂   | Xanthoma    | 111.2             | 64.4           | 59.3  | 97.1                        | 59.8           | 61.6  | 106                | 65.2           | 61.5  |

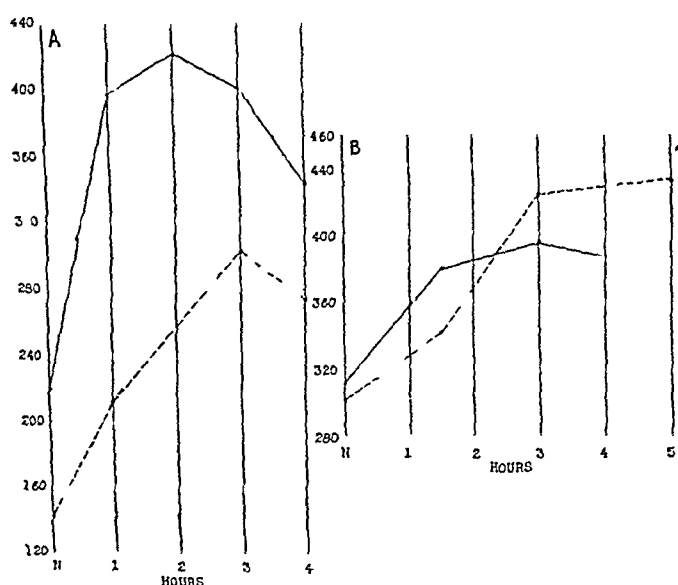


Fig 4—Influence of diabetes on sugar tolerance of skin and blood A, curves of persons with diabetes, B, curves for a dog one week after total pancreatectomy

even in those cases in which the blood sugar has definitely begun to drop by this time. Therefore, the ratio skin sugar to blood sugar is almost 80 per cent at the end of the fourth hour.

Even more pronounced are the disturbances in the course of the skin sugar curve in total pancreatectomized dogs. Due in all probability to the complete deficiency of the pancreas, the skin sugar rises uninterruptedly throughout the duration of the experiment and ultimately reaches definitely higher levels than does the blood sugar (fig 4B).

However, persons with severe diabetes and totally pancreatectomized dogs unmistakably show that the skin sugar curve, following ad-

ministration of glucose, is just as dependent on the pancreas as the blood sugar curve has long been known to be. Table 8 illustrates this fact. Patients with cutaneous manifestations while presenting only slightly increased fasting blood sugar show a high fasting skin sugar (average 82.8 mg per hundred grams). On the other hand, those without cutaneous symptoms reveal only a slight elevation in skin sugar (average 65.5 mg per hundred grams). Therefore the ratio of skin sugar to blood sugar is considerably higher in

TABLE 8—Skin Blood Sugar Ratio in Relation to Skin Lesions in Persons with Mild Diabetes

| Skin Lesions Present |                |  | Skin Lesions Absent |                |  |
|----------------------|----------------|--|---------------------|----------------|--|
| Blood Sugar, Mg      | Skin Sugar, Mg | Ratio Skin Sugar/Blood Sugar, per Cent | Blood Sugar, Mg     | Skin Sugar, Mg | Ratio Skin Sugar/Blood Sugar, per Cent |
| 125                  | 95             | 77.9                                   | 127                 | 69             | 51.3                                   |
| 129                  | 95             | 73.6                                   | 130                 | 67.5           | 51.9                                   |
| 117                  | 80.5           | 68.8                                   | 132                 | 62.5           | 49.3                                   |
| 117                  | 78.5           | 67.5                                   | 135                 | 62.5           | 46.3                                   |
| 125                  | 74.5           | 59.6                                   | 143                 | 66.2           | 46.2                                   |
| 118                  | 67.9           | 57.2                                   |                     |                |  |
| 160                  | 88.1           | 55                                     |                     |                |  |
| Average 127          | 82.8           | 65.7                                   | 133                 | 65.5           | 49.6                                   |

persons with mild diabetes with cutaneous manifestations (65.7 per cent) than in those without such manifestations (49.6 per cent).

While the available material may seem inadequate, the possibility of mere coincidence in these findings appears to be precluded by the regularity with which the sharp rise in the skin sugar level in diabetic persons with cutaneous manifestations, on the one hand, and the absence of any abnormal increase in the skin sugar in those without cutaneous lesions, on the other

hand, could be demonstrated. However, further investigations on greater material will be necessary.

Interesting, too, are the results of studies we carried out on the behavior of the skin sugar following administration of insulin. When we gave animals insulin in doses large enough to bring on severe muscle spasm and death after two hours, we found that the skin sugar and blood sugar curves were fairly parallel, falling steeply at first, then dropping less precipitously. However, the skin sugar could not be depressed below a certain level, even when death was imminent. Thus, in dogs the sugar level dropped more than 50 per cent in the blood and approximately 40 per cent in the skin, in rabbits, close to 75 per cent in the blood and 63 per cent in the skin. Tsukada<sup>17</sup> arrived at similar results (76 per cent and 66 per cent).

#### BEHAVIOR OF THE SKIN AND BLOOD SUGAR IN VARIOUS DISEASES OF THE SKIN

On the basis of our material, we can divide the cutaneous conditions into six distinct groups:

- (1) Cutaneous diseases in which the carbohydrate metabolism is in no way involved (skin sugar and blood sugar curves normal)
- (2) Cutaneous diseases in frankly diabetic patient as evidenced by fasting hyperglycemia
- (3) Dermatoses in persons with latent diabetes, in whom the nature of the disease can be demonstrated only by means of the sugar tolerance test
- (4) Dermatoses in persons with normal fasting blood sugar but with high fasting skin sugar levels (cutaneous glycohistechia,<sup>23</sup> or skin diabetes)
- (5) Skin diseases in persons who may present an atypical blood sugar curve, but who are nevertheless not diabetic, as demonstrated by the normal skin sugar curve
- (6) Skin diseases which are not the result but the cause of increased blood and skin sugar levels, as demonstrated by the fact that both curves return to normal after the dermatosis has been cured by external therapy

The first group is of no concern to us here. In the second group the blood and skin sugar curves show the typical diabetic contours previously mentioned and as exemplified in figure 5. The clinical manifestations include certain forms of eczema, as well as balanitis, pruritus, urticaria, staphylococcal diseases (folliculitis, furunculosis, carbuncles, pyoderma, hidrosadenitis axillaris), monilia infection of the skin, xanthosis, xanthoma, necrobiosis lipoidica diabetorum and gangrene of the toes. Needless to say, only a small percentage of cases of these diseases is attributable to diabetes, except of necrobiosis

lipoidica. However, that diabetic causation must always be borne in mind is shown by the statistics published by von Noorden and Isaac.<sup>24</sup> In their material, which consists of 25,000 diabetic persons, 21.5 per cent of the patients suffered from pruritus at one time or another, while in a group of patients over 50 years of age, from 5 per cent to 8 per cent presented refractory eczema and 10 per cent had furunculosis, carbuncles or acneform eruptions. According to Greenwood,<sup>25</sup> who studied the skin in 500 cases of diabetes at Dr. Joslin's clinic, diabetic patients show a higher incidence of infections of the skin than do nondiabetic persons. This is corroborated by the investigations of Pillsbury and Sternberg,<sup>26</sup> who demonstrated that the course of experimental cutaneous infections is more severe in dogs on a high carbohydrate intake than in those on a low carbohydrate diet.

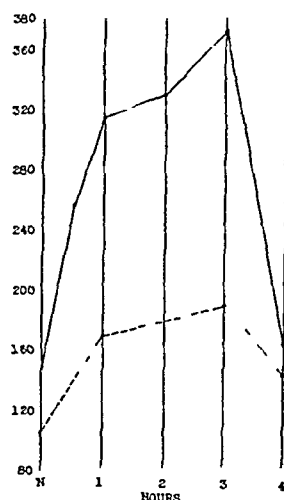


Fig 5—Diabetic sugar tolerance curves of blood and skin in a case of hidrosadenitis axillaris (complicating diabetes)

Group 3 comprises the cases in which the fasting blood and skin sugar appear normal, but in which sugar tolerance tests reveal a diabetic curve. The possibility of latent diabetes should always be borne in mind when the dermatosis presents unusual symptoms such as inordinate severity or extent (e.g., of an eczema or furunculosis), unusual localization (e.g., a dermatitis in the genital regions or in the intertriginous areas, fissures in the corners of the mouth or pruritus vulvae) or failure of the usual thera-

<sup>24</sup> von Noorden, C. H., and Isaac, S. *Die Zuckerkrankheit und ihre Behandlung*, Berlin, Julius Springer, 1927.

<sup>25</sup> Greenwood, A. M. A Study of the Skin in Five Hundred Cases of Diabetes, *J. A. M. A.* **89**: 774 (Sept 3) 1927.

<sup>26</sup> Pillsbury, D. M., and Sternberg, T. H. Relation of Diet to Cutaneous Infection, *Arch. Dermat. & Syph.* **35**: 893 (May) 1937.

<sup>23</sup> (Greek γλυκός = sweet, ιστός = tissue, εχειν = to hold)

therapeutic measures or when the clinical characters of the patient (habitus, age, race) arouse suspicion. Obese persons over 50 years of age, with a somewhat purplish red complexion, are often liable to have latent diabetes, especially when they are of Jewish parentage.

As an example we present the case of an obese woman of 32 who had been suffering from severe urticaria for many months. The sugar tolerance, while starting with normal blood and skin sugar values (fig 6), showed a typical diabetic response. Elimination of carbohydrates from the diet for twenty-four hours caused urticaria to disappear, while it reappeared three hours after three pieces of sugar had been taken in tea. The patient presented no manifestations so long as she adhered to a carbohydrate-free diet.

Similar circumstances have been encountered in a few cases of pruritus and eczema ani, furunculosis, abscesses of the sweat glands, etc.

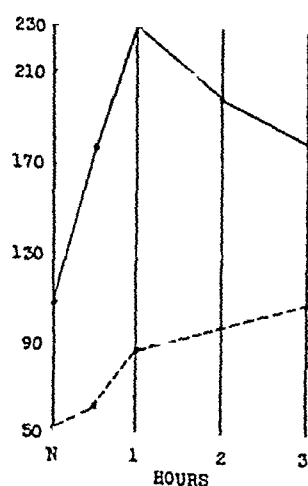


Fig 6—Latent type of sugar tolerance curve of blood and of skin in a case of urticaria in a subject with a prediabetic condition

Group 4 comprises the relatively rare cases in which the blood sugar values are normal while the skin sugar level is well above the normal. This discrepancy becomes even greater following a sugar tolerance test, when the skin sugar curve alone becomes pathologic. One of us (L. U)<sup>2</sup> has coined the term cutaneous glycolistechia, or skin diabetes, to designate this phenomenon. Further details of this interesting phenomenon will be presented in a study soon to be published.<sup>27</sup> For the present we shall limit ourselves to the statement that we should probably include in this group those cases reported by French authors in which insulin treatment was beneficial for refractory ulcers of the skin despite a normal blood sugar curve.

Group 5, on the other hand, comprises the dermatoses in which the sugar tolerance test

<sup>27</sup> Urbach E. Skin Diabetes. Hyperglycemia Without Hyperglycemia, J A M A 129 438 (Oct 6) 1945

shows an enormous rise in the blood sugar level, which returns to normal, however, after three hours. The skin sugar curve (fig 7) in contrast to the blood sugar curve is normal in these cases. Table 9 clearly illustrates the difference between sympathetic-endocrine and diabetic skin sugar curves. In the former there is nothing like the

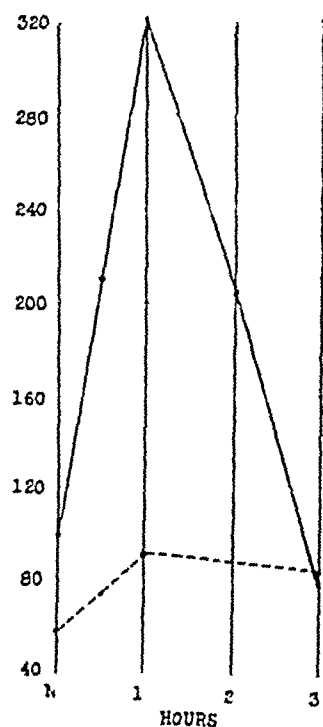


Fig 7—Sympathetic-endocrine blood sugar tolerance curve. Note the lack of parallel between skin and blood sugar curves.

excessive rise shown by the blood sugar curve; the peak is reached during the first hour, and the level returns to the normal between the third and fourth hours. The diabetic skin sugar curve shows considerably higher fasting levels to begin with, it does not reach its much higher peak, however, until the third hour, and takes five hours or more to return to its normal level.

TABLE 9—Difference Between Sympathetic-Endocrine and Diabetic Blood Sugar

|                          | Curves                 |                                     |
|--------------------------|------------------------|-------------------------------------|
|                          | Sympathetic Endocrine  | Diabetic                            |
| Time of peak             | 30 to 60 minutes       | 2 to 3 hours                        |
| Shape of curve           | Sharp rise, steep fall | Flat with prolonged gradual decline |
| Return to starting level | In 2 to 3 hours        | At least 4 hours                    |
| Hypoglycemia             | May occur              | Does not occur                      |

We encountered such atypical blood sugar curves notably in severe ulcers of the skin, in a case of pyoderma chronicum ulcerosum, in several cases of urticaria and others. A common characteristic of these various diseases was then therapeutic refractoriness to a low carbohydrate diet, prolonged administration of insulin and local application of insulin to the ulcers. Therefore,



in conformity with the normal skin sugar curve after a sugar tolerance test, we feel justified in attributing these pathologic blood sugar curves not to a decrease in sugar tolerance but to an excessive mobilization of dextrose (Holsti<sup>28</sup>), probably of endocrine and/or sympathetic origin. This interpretation would also serve to explain the combination of fasting hyperglycemia and elevated basal metabolism or hyperglycemia during a sugar tolerance test, as observed in acne vulgaris by Levin and Kahn<sup>29</sup> as well as by Urbach<sup>30</sup>. This makes understandable McGlasson's<sup>31</sup> observation that patients with neurodermatitis with high blood sugar levels who failed to respond to a diabetic diet or to insulin were cured by a change of climate (in the mountains).

We consider it of great clinical significance that the patients in this group show no improvement whatsoever when put on a low carbohydrate diet and given a long course of treatment with insulin.

We now come to group 6. Disturbances of the carbohydrate metabolism, as evidenced by elevated fasting blood sugar and skin sugar levels and by pathologic blood sugar and skin sugar curves, and attributable to an extensive experimental dermatitis of chemical or mechanical origin, were first demonstrated by Miyake and associates<sup>32</sup>.

According to these authors, the blood sugar and skin sugar are affected because the severe inflammation of the skin leads to the formation of by-products, which either directly or by way of the nervous system affect the cells of the liver and thus bring about an insufficiency of the carbohydrate metabolism. Pillsbury and Kulchar<sup>33</sup> noted in animals that following an injection of dextrose the inflamed skin generally showed a higher sugar level than did normal skin areas.

28 Holsti, O. Studies Concerning Variations of Blood Sugar Reaction in Disease, *Acta med Scandinav* **66** 443, 1927.

29 Levin, O. L. and Kahn, M. Biochemical Studies in Diseases of Skin. Acne Vulgaris, *Am J M Sc* **164** 379, 1922.

30 Urbach, E. Untersuchungen ueber den Energie-stoffwechsel bei Hautkranken, *Arch f Dermat u Syph* **152** 304, 1926.

31 McGlasson, I. L. Hyperglycemia as Etiologic Factor in Certain Dermatoses, *Arch Dermat & Syph* **8** 665 (Nov.) 1923.

32 Miyake, I., and Narahara, K. Eczematoese Hautveraenderung und Zuckerstoffwechsel. Hautzucker und eczematoese Hautveraenderung, *Jap J Dermat & Urol* **30** 85, 1930.

33 Pillsbury, D. M., and Kulchar, G. V. The Dextrose and Water Content of Normal and of Inflamed Skin, *Arch Dermat & Syph* **30** 489 (Oct.) 1934.

The results of these animal experiments seem to conform perfectly with those obtained by Moncorps,<sup>34</sup> Milbradt<sup>35</sup> and Marchionni<sup>36</sup> in their studies of human material. Their investigations reveal that intensive ultraviolet irradiation is followed by a rise in the skin sugar and blood sugar levels and by pathoglycemic sugar tolerance curves.

Noteworthy in this connection are the observations reported by Ayres,<sup>37</sup> Schmidt,<sup>38</sup> Whitfield<sup>39</sup> and others to the effect that pyogenic infections decrease the patient's dextrose tolerance, or at least decrease the rate at which sugar is removed from the blood stream and the tissues. After the dermatosis has cleared up under suitable external treatment it is often found that the blood sugar level has returned to normal. In animal experiments Nicholson and Holman<sup>4</sup> demonstrated that staphylococcal skin infections produced a definite although temporary decrease in carbohydrate tolerance in rabbits, with glucose tolerance curves similar to those seen in mild diabetes.

Similarly Moncorps and Speierer<sup>41</sup> found that in some of their patients with psoriasis who presented abnormal curves following administration of glucose the blood sugar level returned to normal after the eruption had cleared up.

We have been unable to confirm Panti's<sup>41</sup> claim that in psoriasis the sugar content of the skin rises relatively more than does that of the blood.

In summary of this group it may be said therefore, that in man and animals alike extensive inflammations of the skin can exert an influence on the carbohydrate metabolism, which

34 Moncorps, C., Bohnstedt, R. M., and Schmid, R. Ueber den Zucker- und Glutathiongehalt von Blut und Haut bei Hoehensonne- und Crotonoel-dermatitis, *Arch f Dermat u Syph* **169** 67, 1934.

35 Milbradt, W. Der Einfluss der experimenteller Dermatitis auf den Funktionszustand innerer Organe, *Arch f Dermat u Syph* **169** 494, 1934.

36 Marchionni, A. Hautkrankheiten und Stoffwechsel, *Med Welt* **11** 1197, 1937.

37 Ayres, S., Jr. Glucose Tolerance Reactions in Eczema, *Arch Dermat & Syph* **11** 623 (May) 1925.

38 Schmidt, E. G., Eastland, J. S., and Burns, J. H.: Infection and Tolerance for Dextrose, *Arch Int Med* **54** 466 (Sept.) 1934.

39 Whitfield, A. Dermatoses and Nutrition, 9. Internat Dermat Cong **1** 252, 1935.

40 Nicholson, T. F., and Holman, W. L. Carbohydrate Metabolism and Staphylococcus Infection in Rabbits, *Proc Soc Exper Biol & Med* **49** 75, 1942.

41 Moncorps, C., and Speierer, C. Psoriasis und Kohlehydratstoffwechsel, *Arch f Dermat u Syph* **164** 642, 1932.

41a Agostini, A., and Panti, A. Piodermite necrotica con esito letale in soggetto ipoglicemico, *Dermosifilografico* **15** 242, 1940.

means, in other words, that this metabolic disturbance may fundamentally be of peripheral origin. As to the precise manner in which the periphery (e. g., the skin) exerts its influence on metabolism, whether this takes place as a result of an influx of nitrogen or uric acid released in the skin due to increased nuclear disintegration or indirectly via the endocrine glands or via the vegetative nervous system, very little is as yet known. However, some authors have derived substances from artificially inflamed skin which raise the blood sugar level and prolong the sugar tolerance curve. This would seem to demonstrate conclusively that the disturbances in the carbohydrate metabolism which appear in the course of transient dermatoses and disappear when the cutaneous manifestations clear up are in no way connected with pancreatic diabetes.

The practical conclusion to be drawn from these observations is that great care must be taken in evaluating the pathoglycemic results with regard to the pathogenesis and therapy of extensive or inflammatory diseases of the skin. For it is only when antidiabetic treatment (diet and/or insulin) is followed by clinical improvement that the etiologic significance of the disturbance of the carbohydrate metabolism may be regarded as firmly established. Otherwise the metabolic disturbance should be interpreted as a result of the skin disease.

#### ROLE OF THE SKIN IN INTERMEDIARY CARBOHYDRATE METABOLISM

One of us (E. U.) has for years been championing the concept that the skin not only serves as a temporary storehouse of dextrose but also plays an important role in the intermediary carbohydrate metabolism. We submit the following evidence in support of this thesis: (1) the high levels of free and bound sugar in the skin of animals, (2) the demonstrable presence of cleavage and end products of the intermediary carbohydrate metabolism in the skin, (3) the skin's capacity to transform glucose into glycogen, (4) the presence of glycolytic ferments in the skin and (5) the fact that insulin-like substances can be derived from the skin.

(1) Urbach and associates<sup>2, 5</sup> were the first to demonstrate that the skin of almost all animals contains appreciably higher quantities of free sugar than does the blood. These findings have been confirmed by many other authors. Furthermore human and animal skin shows bound sugar levels that are from ten to fifteen times higher than those of the blood (table 3).

Since the bound sugar is to be regarded as the organism's second sugar reserve (Grev-

stuck,<sup>12</sup> Niwa<sup>12</sup>), the high levels in the skin would seem to be the expression not merely of a process of diffusion or of storage but of an active carbohydrate metabolism.

(2) Lactic acid is an important product in the intermediary metabolism of carbohydrates. It is of particular interest to note, therefore, that Fahrig<sup>13</sup> and Wohlgemuth and Ikebata<sup>14</sup> were able to demonstrate that the skin is capable of transforming dextrose into lactic acid *in vitro*. However, it was Pillsbury<sup>15</sup> who established the fact that lactic acid is present in the normal living skin, and that its lactic acid level tends to be low in starved animals and higher in well fed animals, and lastly, that the skin of animals previously given injections of dextrose forms increased amounts of lactic acid *in vitro*. These findings have been confirmed by Moncorps.<sup>16</sup> The quantitative fluctuations of the lactic acid in the skin thus serve as an index of the relative intensity of the carbohydrate metabolism in that tissue.

(3) The fact that investigation with special staining procedures reveals the glycogen in the epithelial sheaths of the hair follicle and in the sebaceous sweat glands, and nowhere else in the skin, is the reason why the presence of glycogen in the skin has long been disputed. Studies with quantitative chemical methods have, however, settled this controversy conclusively. Some time ago Palmer,<sup>17</sup> as well as Urbach and Sicher,<sup>4</sup> mentioned the rapid increase in skin sugar due to postmortem glycogenolysis—a statement inferring the presence of not inconsiderable amounts of glycogen. Fahrig<sup>13</sup> found glycogen values ranging between 226 and 344 mg per hundred grams in the epidermis, and between 71 and 157 in the corium of the human skin. According to Cornbleet,<sup>18</sup> the skin normally contains from 68 to 85 per hundred grams of gly-

42 Niwa, Y. Gebundener Zucker als Zuckerreserve, *Kyoto-Ikadaigaku-Zasshi* 5:25, 1931.

43 Fahrig, C. Ueber den Kohlenhydratumsatz der Geschwulste und ihrer normalen Vergleichsgewebe sowie seine Beziehung zum Milchsäurehaushalt des Körpers, *Ztschr. f. Krebsforsch.* 25:146, 1927.

44 Wohlgemuth, J., and Ikebata, T. Die Fermente der Haut VIII. Ueber Milchsäurebildung in der Haut und ihre Beeinflussung durch verschiedene Strahlenarten, *Biochem. Ztschr.* 186:43, 1927.

45 Pillsbury, D. M. The Intrinsic Carbohydrate Metabolism of the Skin, *J. A. M. A.* 96:426 (Feb. 7) 1931.

46 Moncorps, C. Kohlenhydratstoffwechsel und Haut, *Jahresk. f. arztl. Fortbild.* 22:27, 1931.

47 Palmer, W. W. The Concentration of Dextrose in the Tissues of Normal and Diabetic Animals, *J. Biol. Chem.* 30:79, 1917.

48 Cornbleet, T. Cutaneous Carbohydrates, *Arch. Dermat. & Syph.* 41:193 (Feb.) 1940.

cogen Warren<sup>49</sup> adds the interesting observation that the skin of diabetic patients shows lower levels. Cornbleet<sup>48</sup> established the fact that, while phloisizin poisoning lowers the dextrose levels in the blood and in the skin, it does not affect that of cutaneous glycogen. This shows, once again that skin sugar and glycogen can be mutually independent. The Kaplanskys<sup>50</sup> demonstrated that the skin glycogen curve, following feeding of sugar, presents the direct reverse of the skin sugar curve. Moreover, as Cornbleet<sup>48</sup> has demonstrated, injection of insulin causes the skin's glycogen level to rise and that of the skin sugar to fall. The fact that the sugar concentration is higher in the skin than in the blood of animals is attributed by the Kaplanskys to the glycogenolysis that takes place in the skin. Furthermore these authors are of the opinion that the rise in the skin's glycogen content, accompanied by a decline in skin sugar levels, may be explained by glycogen synthesis in the skin. The skin's high diastase level (130 to 170 mg per hundred grams)—a level that almost approaches that of the liver—suggests the presence of enzymatic activity. On the other hand, Pillsbury and Sternberg<sup>26</sup> state that the glycogen level in the skin of dogs shows only a mild response to variations in the diet (129 mg per hundred grams on a high carbohydrate diet, as compared with 107 mg on a low carbohydrate diet). Narahara<sup>51</sup> observed that in contrast to the great fluctuations in the skin glucose levels following sugar administered by mouth, the skin glycogen levels remained relatively constant. This led Narahara to the conclusion that the skin plays an important role as a temporary receptacle for sugar, but that its role as an organ for permanent storage is rather small.

(4) To date the glycogenolytic and glucolytic enzymes which have been demonstrated in the skin consist in part of hydrolases (such as carbohydrases, amylases, diastases and glucosidases), which split up carbohydrates into simple cleavage products by means of hydrolysis, and desmolases (such as carboxylases, phosphatases, oxidation-reduction systems such as glutathione), which directly attack the carbon chain (Wohlgemuth and associates<sup>52</sup> Melczer,<sup>53</sup> Morcorps<sup>46</sup>). Only

a few of the most important findings will be selected from the great mass of pertinent reports. According to Wohlgemuth<sup>52</sup> the levels of starch-splitting ferment, diastase, are considerably higher in the skin than in the liver, and sometimes even higher than in the blood. It is interesting to note that the skin of animals contains far more diastase than does human skin, which conforms perfectly with the relatively high skin sugar levels in animals. Ottenstein<sup>54</sup> has established the fact that in diabetic persons the fasting blood shows low diastase levels, while they are strikingly high in the skin of the patients.

Wohlgemuth<sup>52</sup> and others demonstrated that the skin, as well as the liver and the muscle form acetaldehyde from carbohydrates and that traces of acetaldehyde can be demonstrated in the freshly excised skin even when no sugar is added. The skin's participation in the oxidation of sugar as established by these investigations must not be underrated when viewed in connection with the role played by the liver in this respect. For it must always be remembered that the skin is a much larger organ, being three times as heavy as the liver and constituting approximately 16 per cent of the total weight of the body. Wohlgemuth has further demonstrated that under suitable experimental conditions the skin is capable of converting phosphorylated sugar into methylglyoxal, and of transforming this in turn into lactic acid. Thus the sugar degradation process goes through the same stages in the skin as in the muscle and liver.

(5) Perutz, Lustig and Klein<sup>55</sup> demonstrated some time ago that the liver is not the only organ responsible for ketogenesis and the results of ketosis, but that the skin also takes part in the process. Midana and Del Grande<sup>56</sup> were able to demonstrate the presence of abnormally high ketone levels in the blood of patients (on a carb

49 Warren, S. The Pathology of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1938.

50 Kaplansky, S. J., and Kaplanskaya-Raykaya, S. J. Carbohydrate Metabolism in the Skin, Arch. biol. Nauk **39** 169, 1935.

51 Narahara, K. Experimentelle Untersuchung ueber den Hautzucker. IX. Hautglykogen und Zuckerabbau in der Haut, Jap. J. Dermat. & Urol. (Abstr. Sect.) **35** 31, 1934.

52 Wohlgemuth, J. Ueber den Kohlehydratstoffwechsel der Haut, Deutsche med. Wchnschr. **57** 181, 1931.

53 Melczer, N. Beitrage zur Kenntnis der Fermente der menschlichen Haut, Dermat. Ztschr. **49** 25, 1927.

54 Ottenstein, B. Untersuchungen ueber den Gehalt der Haut und des Blutes an diastatischem Ferment und dessen biochemische Bedeutung bei Hautkrankheiten. Hautdiastase bei Hautkrankheiten und bei Diabetes. Biochem. Ztschr. **240** 344 and 350, 1931.

55 Perutz, A., Lustig, B., and Klein, A. E. Zentralen Regulation des Fettstoffwechsels der Hautoberflaeche, Arch. f. Dermat. u. Syph. **70** 511, 1934.

56 Midana, A., and Del Grande, L. Ueber den Einfluss der pathologischen Vorgaenge der Haut auf den experimentellen Hyperketonaemie, Arch. f. Dermat. u. Syph. **171** 208, 1935.

hydrate-free diet) who presented an extensive dermatosis but no signs of hepatic changes. The authors conclude, therefore, that the skin is capable of forming ketone bodies under certain pathologic conditions. In this process there is a greater increase in beta-hydroxybutyric acid and aceto-acetic acid. The degree of the increase is dependent on the extent of the cutaneous disease. When the latter improves the ketone level in the blood returns to normal.

Employing a modification of Collip's procedure for obtaining insulin, Moncorps<sup>46</sup> succeeded in deriving a substance from the skin which was found to have the capacity of lowering the blood sugar and skin sugar levels considerably, a substance which bears a close resemblance, at the very least, to insulin. These observations have been confirmed by Milbradt<sup>57</sup> and Reusch<sup>58</sup>. Moreover, Schwarzmnn<sup>59</sup> has reported a similar depressing action on the blood sugar of an aqueous skin extract.

Lastly, the literature contains numerous reports on experimental studies, to the effect that the skin and blood sugar curves need not necessarily run parallel to each other under certain circumstances they can be quite dissimilar, and sometimes even take opposite courses. Thus, one of us<sup>4</sup> observed, in studies on patients with diabetes and on depancreatized dogs, that the rise in cutaneous sugar is both higher and of longer duration than the rise in blood sugar. Urbach,<sup>4</sup> Trimble and Carey,<sup>60</sup> as well as Tsukada,<sup>17</sup> have demonstrated that fatal doses of insulin cause a greater fall in blood sugar than in skin sugar and that it is impossible to depress the skin sugar below a certain level. Similarly, diabetic patients who have been undergoing a long course of insulin therapy and who have at the same time been on a low carbohydrate diet, also show a greater decline in the blood sugar than in the skin sugar level.<sup>4</sup> Furthermore, Seller and Spiera<sup>61</sup> claim that blockade of the reticuloendothelial system, by means of water-blue or gold salts, serves to lower the blood

sugar level, while the skin sugar level is appreciably raised in this manner.

We should like to mention some further facts which show that the skin sugar, more or less independently of the blood sugar, is influenced by certain metabolic factors, a point which once again emphasizes the role of the cutaneous tissues in intermediary carbohydrate metabolism. Thus, Tsukada<sup>17</sup> observed that when rabbits are kept exclusively on a diet of oats they show a relatively higher degree of sugar tolerance, as expressed by the behavior of the skin sugar level, and that, on the other hand, a strict cabbage diet makes for a lower degree of tolerance in this respect. This may probably be explained by the fact that the oat diet makes the skin relatively more acid while the cabbage diet, on the other hand, tends to alkalize it. Lastly, Tsukada found that injections of insulin had definitely less effect on the skin sugar when the animal's diet was acidotic than when it was alkalotic, and that the difference actually went so far that following administration of insulin animals fed oats presented no hypoglycemic manifestations whatsoever, while animals on a cabbage diet responded with severe muscle spasms.

These various facts, which have been arrived at by means of investigations along chemical and biologic lines, clearly point to the probable presence of an intermediary carbohydrate metabolism in the skin, and would also seem to refute the assumption of Folin and associates<sup>62</sup> that a high skin sugar level is to be regarded merely as the result of passive diffusion.

#### COMMENT

In the past few years many authors have investigated the relations between diseases of the skin and carbohydrate metabolism, either by studying the fasting blood sugar levels or by performing blood sugar tolerance tests. Various results have been arrived at in the course of these investigations. Disregarding the question of dermatoses in diabetic patients for the moment, it may now be considered as an established fact that a disturbance of carbohydrate metabolism occurs in only a few cutaneous diseases—certain types of eczema (notably those localized in the intertriginous zones and in the areas surrounding the excretory orifices), staphylococcal diseases, including furunculosis, carbuncles, ecthyma, pyoderma, dermatomycoses (here again notably

<sup>57</sup> Milbradt, W. Ueber das antiallergische und antimetabolische Prinzip im Hautextract, 9 Internat Dermat Cong 1 688, 1935.

<sup>58</sup> Reusch, E. Untersuchung ueber die Wirkung von Hautextrakten auf den Blutzuckerspiegel, Ztschr f d ges exper Med 105 743, 1939.

<sup>59</sup> Schwarzmnn, J. S. Mitteilungen ueber einen Extrakt aus lebender menschlicher Haut, Dermat Wchnschr 103.1210, 1936.

<sup>60</sup> Trimble, H. C., and Carey, B. W., Jr. On the True Sugar Content of Skin and of Muscle in Diabetic and Non-Diabetic Persons, J Biol Chem 90 655, 1931.

<sup>61</sup> Seller, C., and Spiera, M. Die Rolle der Haut im Kohlenhydratstoffwechsel, Biochem Ztschr 296 83, 1938.

<sup>62</sup> Folin, O., Trimble, H. C., and Newman, L. H. Distribution and Recovery of Glucose Injected into Animals, J Biol Chem 75.263, 1927.

those localized in the intertriginous zones), necrobiosis lipoidica, xanthosis, certain forms of xanthelasma, and, lastly, many cases of pruritus. It must always be borne in mind, however, that disturbances in the carbohydrate metabolism are not infrequently a result of pathologic changes in the skin.

As mentioned in the beginning of this paper, one of us (E. U.) has long supported the view that analysis of the blood alone cannot by any means afford a clear picture of the chemistry of healthy or diseased skin tissue, and that, on the other hand, a study of biopsy specimens is essential for this purpose. A similar view is held by Barat and Hetényi,<sup>63</sup> who were able to demonstrate that the blood sugar level does not in itself constitute a dependable index of the sugar retention in the muscle tissue of diabetic patients. Pollak<sup>64</sup> also pointed out that the blood sugar level does not by any means offer a guide for measuring the quantity of free dextrose which may temporarily be present in the organism. Furthermore, Barat and Hetényi<sup>63</sup> found in studies on corpses that the organs of diabetic and of nondiabetic persons could be differentiated by the higher sugar levels in the former, and that in cases of hyperglycemia of nondiabetic origin the tissue sugar levels were not abnormally elevated.

Similarly, Urbach and Sicher<sup>4</sup> established the fact in cases of so-called sympathetic endocrine hyperglycemia (fig. 7) that the skin sugar curve in no way takes part in this rise, an observation which further proves that the enormous rise in blood sugar level is not of diabetic origin.

It is true that the great rise in blood sugar which generally takes place during the sugar tolerance test in human beings or animals on a low carbohydrate diet is accompanied by a corresponding rise in the skin sugar levels, but both levels return to normal speedily, while they remain elevated for some time in diabetic subjects.

Lastly, there is the type of case which presents hyperglycoderma without hyperglycemia. In such cases the eruption does not yield to therapy until the patient is put on an antidiabetic diet.

It is, therefore, essential to carry out determinations of the skin sugar in all doubtful cases in which the presenting cutaneous disease might possibly be attributable to a disturbance in the carbohydrate metabolism. We call this method

"chemical biopsy" of the skin. While it has been demonstrated again and again that certain dermatoses are the consequence of a disturbance of the carbohydrate metabolism, the nature of the pathogenesis involved is still a highly controversial question. The following more or less well founded theories have been advanced to explain the connection.

(1) The increased concentrations of sugar, or of an intermediary product of the carbohydrates, in the skin act in one of three ways: by direct stimulation of the sensory nerves of the skin, causing pruritus, by creating a disturbance of the secretory and vasomotor nerves, resulting in anhydrosis, asteatosis and xerosis of the skin, or by exerting a direct influence on the capillary walls and glands (Kaposi).<sup>64</sup>

(2) J. Jadassohn<sup>65</sup> regards some of the cutaneous diseases in diabetic patients as belonging to the group of excretory dermatoses, on the theory that the sugar passing through the secreting glands exerts a pathogenetic influence on the skin's bacterial flora. Carrie and Koenig<sup>66</sup> have demonstrated that patients with high blood sugar levels excrete abnormally large amounts of sugar onto the skin surface.

(3) Abnormal decomposition products of sugar bring about an "Umstimmung" (transformation of the terrain) as a result of which the skin reacts to endogenous and exogenous stimuli other than those derived from the abnormal sugar metabolism, with cutaneous manifestations (Bloch,<sup>67</sup> Achard<sup>68</sup>).

(4) According to Stokes, Beerman and Ingraham<sup>69</sup> ingested carbohydrate may influence infections of the skin through its action on the bacterial content of the intestinal tract, causing vasomotor instability which constitutes a clinically important factor predisposing to a wide variety of inflammatory reactions.

(5) The influence of carbohydrate on infections of the skin may be exerted through its effect on the water balance of the tissues. For a high carbohydrate intake leads to retention

65 Jadassohn, J. *Hautkrankheiten bei Stoffwechselanomalien*, 5. Internat. Dermat. Cong. 2: 155, 1905.

66 Carrie, C., and Koenig, R. *Ueber den Zuckergehalt auf der Haut bei Normalen und Diabetikern*, Arch. f. Dermat. u. Syph. 173: 611, 1936.

67 Bloch, B. *Beziehungen zwischen Hautkrankheiten und Stoffwechselanomalien*, Ergebn. d. inn. Med. 2: 521, 1908.

68 Achard, C. *Cinque leçons sur le diabète*, Paris, Masson & Cie, 1925.

69 Stokes, J. H., Beerman, H., and Ingraham, N. R., Jr. *Carbohydrate and Water Metabolism and the Vitamins in Skin Inflammation*, Am. J. M. Sc. 195: 562, 1938.

63 Barat, I., and Hetényi, G. *Zuckerbestimmungen im menschlichen Blut und Gewebe bei Diabetikern*, Deutsches Arch. f. klin. Med. 141: 358, 1922-1923.

64 Pollak, L. *Physiologie und Pathologie der Blutzuckerregulation*, Ergebn. d. inn. Med. 23: 337, 1923.

of water in the tissues (Pillsbury and Sternberg),<sup>26</sup> while carbohydrate restriction results in dehydration followed by decreased susceptibility to experimentally induced cutaneous infections (Kulchar and Alderson<sup>70</sup>)

(6) Rudy and Hoffmann<sup>71</sup> champion the theory that cutaneous manifestations in diabetes mellitus are not related to the hyperglycemia but attributable to the skin's increased vulnerability resulting from a deficiency in the components of the vitamin B complex, notably nicotinic acid. These authors, as well as Gross,<sup>72</sup> report that lesions of the skin, including those of monilia infections in persons with diabetes, respond to treatment with vitamin B complex in addition to nicotinamide. However, since Neuwahl<sup>73</sup> has demonstrated that nicotinic acid improves the carbohydrate tolerance of diabetic patients and may enhance the action of insulin, the therapeutic effect of nicotinic acid and therefore, of course, the explanation based on this effect may not quite conform with Rudy and Hoffmann's views on the subject.

(7) Disorders of the skin involving extensive dermatitis of chemical or mechanical origin may bring on a disturbance in the carbohydrate metabolism. This is generally interpreted as evidence of injury to the liver, rather than as a sign of disturbed pancreatic function (Milbradt<sup>35</sup>).

(8) Lastly, Whitfield<sup>39</sup> alludes to the assumption that in many bacterial infections the thyroid-adrenal apparatus is brought into action as a part of the organism's defense mechanism. The resulting rise in the blood sugar is, therefore, an effect and not the cause of the cutaneous disease.

#### SUMMARY

Chemical analysis of the blood does not in itself suffice to give a clear insight into the physiologic and pathologic mechanism of the skin. For this purpose the living skin must be subjected to a chemical investigation. This can readily be done by means of the electric punch biopsy method, and corresponding microchemical methods now make it possible to undertake a series of biopsies.

<sup>70</sup> Kulchar, G. V., and Alderson, H. E. Relation of Water Metabolism to Experimental Skin Infections, *Brit J Dermat* **48** 477, 1936.

<sup>71</sup> Rudy, A., and Hoffmann, R. Skin Disturbances in Diabetes Mellitus. Their Relation to Vitamin Deficiencies, *New England J Med* **227** 893, 1942.

<sup>72</sup> Gross, P. Nonpellagrous Eruptions Due to Deficiency of Vitamin B Complex, *Arch Dermat & Syph* **43** 504 (March) 1941.

<sup>73</sup> Neuwahl, F. J. Action of Nicotinic Acid on Carbohydrate Metabolism, *Lancet* **2** 348, 1943.

While in human beings the free sugar content of the skin is only two thirds of that of the blood, the skin of many species of animals contains more free sugar than does their blood. Therefore results obtained in experimental investigations on animal skin are not automatically applicable to conditions in human beings.

The bound sugar content of the skin in human beings is about one and one half times that of the blood.

The sugar level of the skin is dependent on the nature of the diet. The same is true, although to a lesser extent, of the blood sugar. The individual who has been on a low carbohydrate diet shows definitely subnormal skin sugar levels, and he may well show low blood sugar levels as well. This fact clearly explains the efficacy of a low carbohydrate diet in diabetic dermatoses. It is interesting to note that the mean blood sugar and skin sugar levels in Philadelphians are lower than those in Viennese, whose diet is much higher in carbohydrate than the usual American diet.

A diet high in fat results in a distinct decrease in the sugar content of the skin while that of the blood remains practically stationary.

A blood sugar tolerance test is indispensable in order to answer the question whether or not a given dermatosis is of diabetic origin. However, the type of curve resulting indicates whether a given pathologic reaction is brought on by excessive mobilization of glucose by an imbalance in the sympathetic or the endocrine system, or by a decrease in the capacity to assimilate sugar, i. e. by a lowered sugar tolerance, as in diabetes.

Under normal conditions there is a certain parallelism between the skin sugar and the blood sugar tolerance curves with the one difference that the skin sugar curve reaches its maximum later and, correspondingly, takes longer to return to its original level.

Under pathologic conditions the skin is capable of containing more sugar and for a longer period of time, a fact which seems highly significant when one recalls that the skin constitutes 16 per cent of the total weight of the body and that the skin is three times as heavy as the liver.

In cases of pancreatic diabetes the ratio between the fasting skin sugar and the blood sugar is increased. Moreover, the sugar content of the skin is almost doubled after a sugar tolerance test. Lastly, it takes the skin sugar level five hours or even longer to return to normal. This gives the diabetic skin sugar curve its unmistakably characteristic appearance. The

prolonged and intensive storage of sugar in the skin may, perhaps, explain its great susceptibility to infection in diabetes. In mild diabetes with cutaneous manifestations the ratio of skin sugar to blood sugar is relatively high (65.7 per cent), whereas the ratio is rather low in cases without cutaneous symptoms.

Extensive inflammation or infection of the skin can produce a metabolic disturbance of the carbohydrate metabolism which is fundamentally of peripheral origin and in no way connected with pancreatic diabetes.

Under certain conditions there can be hyperglycoderma without hyperglycemia (cutaneous glycolistechia or cutaneous diabetes).

These facts together with the demonstration of the presence of cleavage and end products of intermediary carbohydrate metabolism in the skin, as well as the presence of glycolytic enzymes in the skin and the fact that insulin-like substances can be derived from cutaneous tissue would seem to underscore the important role played by the skin both in intermediary carbohydrate metabolism and as a storage organ.



# EPIDERMOLYSIS BULLOSA

## A SUGGESTION AS TO POSSIBLE CAUSATION

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Epidermolysis bullosa, a comparatively rare dermatosis, was first recognized as an entity in 1879 by Tilbury Fox<sup>1</sup> Goldscheider,<sup>2</sup> three years later, gave it the name it bears at the present time. Since then most observers have classified the disease into two main groups, namely the simple and the dystrophic forms. The simple form is characterized by the appearance of bullae on the skin, usually without changes in other ectodermal structures such as the teeth, hair and nails, whereas the changes in these appendages is the predominant feature of the dystrophic form. The dystrophic form of the disease has been further subdivided into two types based on hereditary transmission, as a dominant or as a recessive characteristic. Clinically, the dominant dystrophic type is intermediate in severity between the simple and the recessive dystrophic type. The nails may be thickened, clawlike, or absent, but as a rule the teeth and hair are sound, as is the general health of the affected person. In the recessive dystrophic type, on the other hand, severe abnormalities of all the ectodermal structures are evident, lesions of the mucous membranes are frequent since slight trauma will produce them, and the constitutional state of the victims is such that they seldom attain maturity.

The existence of a nonhereditary form of the disease was recognized as early as 1895.<sup>3</sup> In 1915 in an excellent review of the subject Wise and Lautman<sup>4</sup> summarized the literature and bibliography to that date, citing cases collected from the literature, along with 1 of their own, in most of which symptoms were not evidenced until a comparatively late age. Within recent years, Hund-

ley and Smith,<sup>5</sup> Franks and Davis,<sup>6</sup> and Waisman<sup>7</sup> have reported cases corroborating the existence of an acquired type of the disease.

While epidermolysis bullosa is a comparatively rare entity, we believe a somewhat higher incidence is to be expected among military personnel. This is due to several factors: the increased susceptibility of soldiers to trauma, particularly that caused by prolonged marching, and the fact that many minor illnesses, often ignored in civil life, are promptly brought to the attention of medical officers. Greenberg<sup>8</sup> observed 5 cases of epidermolysis bullosa in a total of 2,281 cases seen on the Dermatologic Service at Camp Croft, South Carolina. It is partly to focus attention on this condition that we present the following case.

### REPORT OF A CASE

A Negro private, aged 33, was admitted to the hospital on July 18, 1944 because of recurrent blisters on the right sole. These blisters were first noticed by the patient two years previously following prolonged walking, were subject to exacerbations and were most severe during the warmer months of the year. The bullae were moderately painful only on the first day or two following their appearance, and there was no pruritus. A moderate hyperhidrosis was sometimes evident.

The previous medical history was noncontributory with the exception of hospitalization for previous atypical pneumonia in April 1943. Despite a careful investigation of the family unit, no history of any similar bullous or vesicular lesions in any other member could be elicited, nor was there consanguinity of the parents.

On the plantar surface of the right foot there were numerous discrete, nonerythematous vesicles and bullae, varying in size from approximately 0.4 cm to 1.2 cm. The lesions were predominantly located on the weight-bearing surfaces of the foot, the metatarsal area and the large toe; they were unilocular, thin-walled, only mildly tender and filled with a clear, thin, yellowish, serous

1 Fox, T. Notes on Unusual or Rare Forms of Skin Disease. IV. Congenital Ulceration of the Skin (Two Cases) with Pemphigus Eruption and Arrest of Development Generally, *Lancet* **1** 766, 1879.

2 Goldscheider, A. Hereditäre Neigung zur Blasenbildung, *Monatsh f prakt Dermat* **1** 163, 1882.

3 Elliot, G. T. Two Cases of Epidermolysis Bullosa, *J Cutan & Genito-Urin Dis* **13** 10, 1895.

4 Wise, F., and Lautman, M. F. Epidermolysis Bullosa Beginning in Adult Life. The Acquired Form of the Disease, with the Report of a Case and Review of the Literature, *J Cutan Dis* **33** 44 (June) 1915.

5 Hundley, J. L., and Smith, D. C. Epidermolysis Bullosa Acquisita, *South M J* **34** 36, 1941.

6 Franks, A. G., and Davis, M. I. J. Epidermolysis Bullosa, *Arch Dermat & Syph* **47** 647 (May) 1943.

7 Waisman, M. Recurrent Bullous Eruption of Feet and Hands (Weber-Cockayne). Localized Epidermolysis Bullosa, *J A. M. A* **124** 1247 (April 29) 1944.

8 Greenberg, S. T. Epidermolysis Bullosa, *Arch Dermat & Syph* **49** 333 (May) 1944.

fluid Nikolsky's sign was negative. At the site of previous lesions there was a mild hyperpigmentation, but no atrophy. No gross abnormalities of the hair or teeth were present. The nail of the large toe showed moderate hypertrophy with accumulation of brown corneous material beneath it, but no pitting, longitudinal striation or onychogryphosis was found. The fourth and fifth toes showed similar changes of a lesser degree, but all of these findings in the nails were interpreted as being consistent with the normal in persons of this race and status. At no time were any lesions discoverable elsewhere, and the mucous membranes were clear. The general medical examination gave negative results. Examination of the lower extremities revealed no gross abnormalities other than cutaneous changes. Although no definite measurements of the length of the extremities were taken, the examiners felt that no discrepancies were evident. Varicosities were neither visible nor pal-

In the lower central margin of the epidermic cyst there was a break in the continuity with liberation of a cellular infiltrate, consisting mostly of lymphocytes and mononucleated cells, and an attempt at blood vessel formation. In the upper part of the corium there was a moderate inflammatory reaction consisting chiefly of lymphocytes, plasma cells and mononucleated cells. The infiltrate was predominantly localized around dilated blood vessels and extended into the papillae. There was some disorganization of the connective tissue elements in the corium with a tendency to separation of the fibers, with vacuolation.

#### ETIOLOGIC CONCEPTS

There have been many and divergent theories put forth in an attempt to explain satisfactorily the cause of this disease. Whether there is a common etiologic basis for the acquired and the hereditary forms has been the subject of considerable discussion and doubt. The concomitant presence of hyperhidrosis in some of these cases often has been considered of etiologic significance, however, in many instances excessive sweating is not seen, and certainly in our case hyperhidrosis was a symptom of relatively little importance. It seems more likely that this symptom is a secondary manifestation, an effect of the disease rather than the cause. It would be of interest in this regard to determine accurately whether the so-called hyperhidrosis that is allegedly frequently associated with epidermolysis bullosa is a true hyperhidrosis. Is it a true excess secretion of the coil glands or is it merely a diffuse leakage of serum through inherently defective cutaneous vessels? Studies of acidity of the fluid might be helpful. An endocrine basis for the disease has been advanced by some authors, with almost every ductless gland implicated by one observer or another. Pasini,<sup>9</sup> Drouet,<sup>10</sup> Bonaduce<sup>11</sup> and Kaftan<sup>12</sup> have implicated a thyroid dysfunction as responsible, Longo,<sup>13</sup> Stuhmer<sup>14</sup> and Marcozzi<sup>15</sup> believed a



Fig 1—Epidermolysis bullosa (Photographed by Army Air Forces)

pable. The dorsalis pedis and posterior tibial arteries were easily felt, and were of normal consistency. No changes in temperature at any level of the extremities were noted. Repeated urinalysis and blood counts were normal, the basal metabolic rate was + 5 per cent and the blood calcium 9.4 mg per hundred cubic centimeters. Several Kahn tests were negative. On six different occasions, examinations of the bullae did not reveal fungi, and repeated cultures of the bullous fluid failed to show a growth. The trichophytin test was also negative.

**Histopathologic Description**—The section showed mild hyperkeratosis and a minimal degree of parakeratosis. The stratum corneum, containing ill defined vesicles, was separated from the granular layer by a vacuolar process. In the central portion of the slide there was a large epidermic cyst extending from the granular layer to the basal layer of the epidermis. The cyst was partially filled with fibrinous material and a few lymphocytes.

9 Pasini, A. Epidermolisi congenita bollosa edo albo-papuloide, *Gior ital di dermat e sif* **73** 125, 1932.

10 Drouet, L. Endocrimides cutanees (sclérodémie, epidermolyse bulleuse) chez un myxoedemateux, *Bull Soc franç de dermat et syph* **35** 503, 1928.

11 Bonaduce, F. Osservazioni comparative sopra diversi casi di pemfigo traumatico congenito ed infantile, *Gior ital di dermat e sif* **67** 761, 1926.

12 Kaftan, F. Ein Fall der Epidermolysis bullosa hereditaria mit typischen Erscheinungen im Munde und an den Zähnen, *Deutsche Monatschr f Zahn* **43** 165, 1925.

13 Longo, P. Distrofia cronica della pelle a tipo di epidermolisi bollosa, *Arch ital di dermat e sif* **2** 449, 1927.

14 Stuhmer, A. Ueber Epidermolysis bullosa congenita (Dystrophia cutis spinalis congenita), *Arch f Dermat u Syph* **121** 568, 1918-1919.

15 Marcozzi, A. Epidermolisi bollosa distrofica con ematoporfirinuria ed alterazione endocrinosimpatica, *Arch ital di dermat e sif* **4** 555, 1929.

combination of thyroid and suprarenal imbalance played an important part, while Hudelo and Moutlour<sup>16</sup> and Beinbauer<sup>17</sup> have implicated the gonads. Schwartz and Levin<sup>18</sup> presented 1 case in which the disease seemed to improve following the administration of parathyroid extract and calcium lactate. Association of porphyria and epidermolysis has been noted, but the work of Turner and Obermayer<sup>19</sup> discounted this factor as being of etiologic significance. The suggestion that allergy played a role was made by Ludy, Devalin and Drant,<sup>20</sup> who noted a lessened tendency to formation of bullae in 2 cases, after elimination of certain articles of diet. The experiments were not controlled nor was sufficient observation made over a long enough period for these authors to advance any definite theory.

application of chromic acid to the skin at sites of predilection. It is well known that chromic acid is one of the more frequent sensitizing agents in the pathogenesis of shoe leather dermatitis. Since Luthlen does not mention the concentration of chromic acid used to elicit this phenomenon, it is more than likely that he was dealing with primary irritation rather than true sensitization, and that the same phenomenon could occur in cases other than epidermolysis bullosa. Hemolytic streptococci, group G Lancefield, were isolated from bullae and found to be pathogenic for mice by Cannon, Sanders and Rankin.<sup>22</sup> This organism was isolated by these authors in almost pure culture from the lesions in 4 cases, and their patients showed definite clinical improvement with administration of sulfanilamide, locally and by mouth. It is our impression,

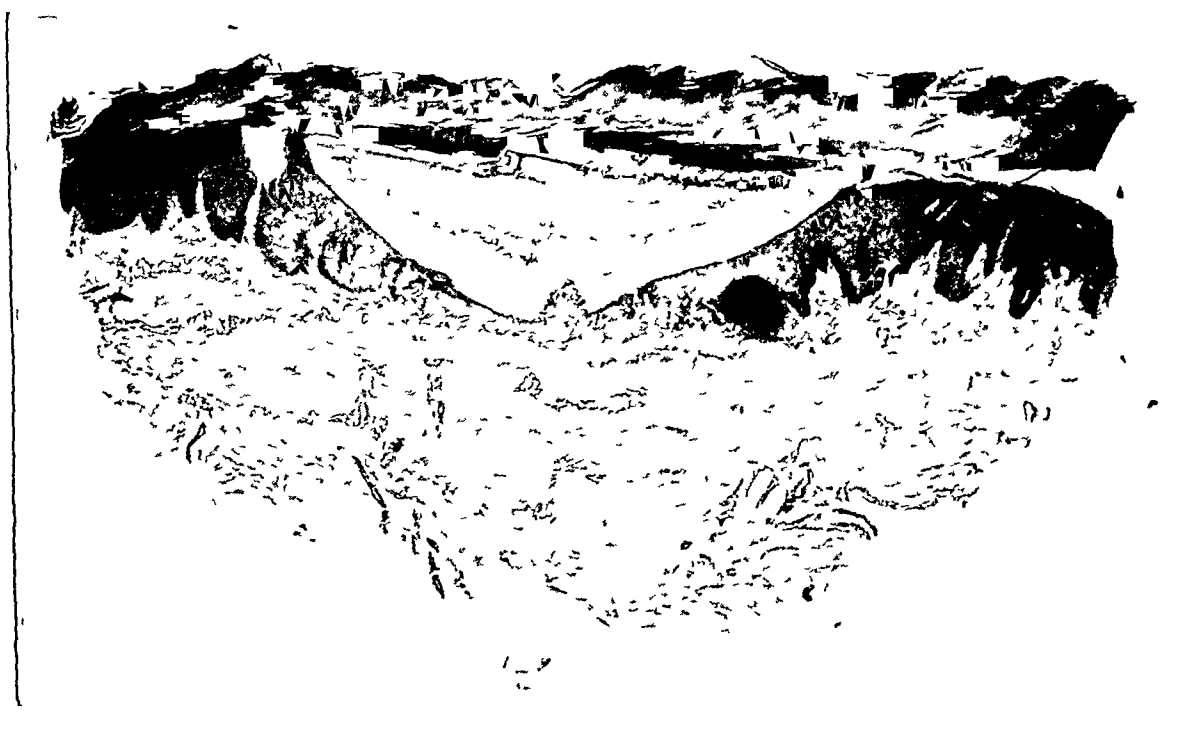


Fig 2—Epidermolysis bullosa (Photographed by U S Army Medical Museum)  $\times 16$ .

It is of interest that in cases of epidermolysis bullosa showing primarily lesions of the feet that Luthlen<sup>21</sup> mentions the artificial production of bullae in epidermolysis bullosa by the

however, that the cultures in these cases were due to a secondary infection, since no subsequent reports have been published to our knowledge and since various bacteria have been cultured from both normal and abnormal skin.

A congenital absence of elastic tissue was found in histologic studies made by Engman and Mook.<sup>23</sup> They found a definite deficiency

16 Hudelo and Moutlour, cited by Petges, G, and Lecoulant, P, in Darier, J, and others, *Nouvelle pratique dermatologie*, Paris, Masson & Cie, 1936, vol 6.

17 Beinbauer, L G. Treatment of Epidermolysis Bullosa, *Arch Dermat & Syph* 32 469 (Sept) 1935.

18 Schwartz and Levin, cited by Sutton, R L, and Sutton, R L, Jr. *Diseases of the Skin*, ed 10, St Louis, C V Mosby Company, 1939.

19 Turner, W J, and Obermayer, M E. Studies on Porphyria. II. Case of Porphyria Accompanied with Epidermolysis Bullosa, Hypertrichosis and Melanosis, *Arch Dermat & Syph* 37 549 (April) 1938.

20 Ludy, J B, Devalin, C M, and Drant, P. Epidermolysis Bullosa, *M Clin North America* 16 169, 1932.

21 Luthlen, F. Epidermolysis Bullosa Hereditaria, in Mracek, S. *Handbuch der Hautkrankheiten*, Vienna, A Holder, 1902, vol 7, p 738.

22 Cannon, A B, Sanders, M, and Rankin, J L, Jr. Epidermolysis Bullosa, A Clinical and Bacteriologic Study, Report of Four Cases, *Arch Dermat & Syph* 42 884 (Nov) 1940.

23 Engman, M F, and Mook, W H. A Study of Some Cases of Epidermolysis Bullosa, with Remarks upon the Congenital Absence of Elastic Tissue, *J Cutan Dis* 24 55, 1906.

of elastic tissue in the papillary and subpapillary layers of the cutis, not only in the area affected by bullous lesions but also in regions apparently normal. On the basis of their findings it was suggested that there occurred a leakage of serum and the production of bullae due to separation of the cutis from the epidermis, at the most vulnerable portions. They believed that this diminution of elastic fibers accounted for the increased susceptibility of these patients to trauma. According to Wise and Lautman,<sup>4</sup> however, the uninjured skin was found to be normal in a case of the acquired type of the disease.

There is considerable substantiation in dermatologic literature for the theory that some disturbance of the vascular system underlies the disease. Whether this disturbance is in the nature of an actual structural change of vascular endothelium or whether it is due to some autonomic nervous imbalance has only been theorized, but in either case many observers have stated their belief that increased permeability of vessel walls occurs with transudation of serum into the upper part of the epidermis, with consequent production of bullae. Elliot<sup>3</sup> states that the prime feature in the pathogenesis of epidermolysis bullosa rests in "an acquired or hereditarily exaggerated irritability of the cutaneous vascular system," a belief which was also shared by Unna<sup>24</sup> and Torok.<sup>25</sup>

With the theory of a basic disturbance of the cutaneous-vascular system in mind, several experimental procedures were attempted with our patient.

#### METHOD

(1) On July 24, 1944 an area of normal skin 1.5 inches (3.8 cm) wide on the medial plantar surface of the right foot was moderately traumatized by stroking with the dull end of a curet for thirty seconds. The area was encircled with white photo ink. No lesions were seen to appear in this area within an observation period of forty-eight hours. On July 26 greater trauma was inflicted on the same area by a steady stroking lasting thirty seconds, followed by an interruption of thirty seconds, the entire cycle being repeated twenty-four times. Again, after a forty-eight hour period of observation no bullae were seen.

(2) On July 28, 0.1 cc of a triple typhoid vaccine (containing one billion organisms of *Bacillus typhosus* and two hundred and fifty million organisms each of the paratyphoid bacilli A and B per cubic centimeter) was given intravenously. Three and one-half hours later the patient exhibited his most decided temperature response, 101.6 F (oral). At this point, the preceding traumatizing procedures with the dull end of a curet were repeated, again with negative results.

24 Unna, P. G. Ueber die Duhringsche Krankheit und eine neue Form derselben, *Dermat Wehnschr* 9, 1889.

25 Török, L. Epidermolysis hereditaria bullosa (Koebner), *Arch f Dermat u Syph* 47, 402, 1889.

(3) Beginning on July 31 the patient was allowed to walk for varying periods of time, under close supervision of a ward attendant, and it was determined that the minimal threshold time for the appearance of bullae was ten minutes. That is, after shorter periods of walking no lesions were found, but after walking for ten minutes from 7 to 8 bullae appeared on the original site after twenty-four hours. This threshold time was verified on several trials.

(4) On August 10 the patient was instructed to stand and rock backward and forward on the heels and toes of both feet. This was done one hundred times, with each forward and backward motion lasting two seconds. After twenty-four hours five new bullous lesions appeared on the ball of the right foot and on the plantar surface of the right large toe.

(5) On August 15, with the threshold time for the appearance of lesions determined and verified as being ten minutes, we attempted to see what proportion of the symptoms was dependent on autonomic nervous factors. The patient was given intravenously 7½ grains (0.49 Gm) of sodium amytal in 10 cc of sterile distilled water, by Capt. George Jervis, base psychiatrist. Seven minutes after the injection had been completed the patient was under mild to moderate narcosis. He was then supported lightly under each arm and instructed to walk for ten minutes. Twenty-four hours following this procedure five bullae were noted on the right sole. Incidentally, while the patient was narcotized an attempt to elicit any possible psychogenic factors was made by Captain Jervis, with completely negative results.

(6) On August 18 a tourniquet was applied below the right knee with moderate pressure. As it was impossible to determine accurately the amount of pressure used, and as the pressure was of the approximate degree one would use in applying a tourniquet for the purpose of withdrawing blood from the cubital vein in the arm, we felt that the pressure was exerted on the venous system primarily. Under observation by a ward attendant, the patient walked with the tourniquet intact for a period of fifteen minutes. The tourniquet was then removed and the patient put to bed. After twenty-four hours not a single new lesion was seen on the foot. On the following day this procedure was repeated. This time the patient walked for twenty minutes, and in place of the tourniquet an elastic bandage was applied from the right ankle to the knee. Again no lesions were seen twenty-four hours following removal of the bandage and placing the patient in bed.

(7) On August 20 the elastic bandage was reapplied and continuously left in place for three days. The patient was instructed to be up and about. The bandage was then removed and the patient returned to strict rest in bed. Despite considerable walking during the three day period that he wore the bandage, only one vesicle appeared on the plantar surface of the fifth right toe.

(8) On August 25 the patient was allowed to walk around the ward during the entire day without the elastic bandage in place. On the next day eight new vesiculobullous lesions were seen.

(9) To allow for possible factors of chance and coincidence, for eighteen consecutive days the patient walked freely about the ward, one day with the elastic bandage in place and the next day without it. On each of these trials the results were exactly the same. That is, no new lesions were seen after each day's walking with the bandage applied, whereas new lesions, usually num-

ering six to eight, appeared the day after he had walked without wearing the bandage

(10) After allowing for partial involution of lesions and encircling any present with white photo ink, on October 3 the patient was made to wear the bandage continuously for a period of one week. During this period he had complete freedom of the ward. Despite considerable walking during this one week interval, only two lesions appeared at the end of this time.

(11) As a final check the elastic bandage was removed, and on October 10 the patient was allowed to walk freely again. Daily observation for a period of five days failed to reveal any new lesions. This was the first finding that was inconsistent with the previous ones. It may be noted, however, that the mean temperature for this five day period was only 59.8 F, whereas the mean temperature for the period in which the foregoing procedures were done averaged 73.5 F, a difference of 13.7°.<sup>26</sup> It is well known that the incidence of bullae formation in epidermolysis bullosa decreases greatly during the colder months of the year. No further observations could be made since the patient was subsequently given a medical discharge from the service.

#### COMMENT

On analysis of these findings it was seen that with the wearing of an occlusive bandage, such as an elastic bandage or a tourniquet exerting only moderate pressure, the threshold of blister formation was considerably increased. Luthlen,<sup>21</sup> in his "Handbuch der Hautkrankheiten," observed that if one uses an Esmarck bandage to empty the extremity of blood no production of bullae results until the bandage is removed. This tends to support the contention of Elliot<sup>3</sup> that there is an underlying disturbance of the cutaneous vascular system in the pathogenesis of the disease. Where, however, is the original site of the disturbance? Engman and Mock<sup>23</sup> believed that a lack or scarcity of elastic tissue in the papillary and subpapillary layers of the cutis brought about a leakage of serum with the production of bullae in areas exposed to trauma. But, as Wise and Lautman<sup>4</sup> have shown, no deficiency of elastic tissue occurs in normal areas of skin of patients with epidermolysis bullosa.

Can the primary disturbance be due to an altered control of vascular tone by the autonomic nervous system, with attendant transudation of serum? It is beyond the scope of this paper to rule out all the factors which might cause an autonomic imbalance. An attempt was made, however, to determine whether some psychogenic factor played a part. This was suggested by

the work of Goldman, Nelson and Mirsky,<sup>27</sup> who found that under pentobarbital sodium anesthesia the skin of ducks was much less susceptible to the production of vesicles by mustard agent. In our patient, however, one induction of narcosis by sodium amytal was completely ineffectual and no significant psychogenic factors could be elicited by a competent psychiatrist.

It is our impression, gained on the basis of observations in the case presented, that some inherent defect of the vessel wall itself may constitute the primary cause of epidermolysis bullosa, at least in the acquired form of the disease. Whether this likewise applies in the hereditary form is purely speculative, but it seems a not unlikely possibility. This inherent defect must be of such nature that no clinical signs of any vascular deficiency are ordinarily manifested. The added factor of muscular exercise, however, is sufficient to provoke the production of bullous lesions. In some manner, which we are not prepared to explain, the application of a tourniquet or elastic bandage must overcome the defect present and prevent the appearance of lesions. It appears that artificial trauma, with resultant transitory hyperemia, is not analogous to the muscular action of walking, for stroking with a blunt instrument did not produce bullae in our patient.

We should like to suggest that further vascular studies be carried out in cases of epidermolysis bullosa in an attempt to determine the site and mechanism of the underlying pathologic condition. Study of venous pressures, infra-red photography, venograms and biopsies of the vascular tree might contribute much to the knowledge of the pathogenesis of this condition.

#### SUMMARY

1 A case of simple acquired epidermolysis bullosa in a Negro is presented.

2 Corroborative evidence is brought forth for the theory that some defect of the vascular mechanism is primarily responsible for the manifestations of the disease.

3 It is shown that a diminished tendency to blister formation is achieved through the use of compressive bandages.

4 A plea is made for further experimental studies of the vascular system in this disease.

27 Goldman, L., Nelson, N., and Mirsky, A. I. Production of Bullae in the Skin of the Duck. II. Experiments with Bullae Produced by Vesicants, Arch. Dermat. & Syph. 48:616 (Dec.) 1943.

<sup>26</sup> Army Air Force Base Weather Station, Barksdale Field, Louisiana.

# ACNE VULGARIS OCCURRING IN THE TROPICS IN A PIGMENTARY AND PILOSEBACEOUS NEVUS

COMMANDER HERMAN V ALLINGTON (MC), USNR

Acne vulgaris is one of the many cutaneous diseases which has commonly been noted to flare up in Naval and Marine Corps personnel on duty in the tropics. This has been true aboard ship and at well established bases as well as under field conditions. The constant heat and increased humidity resulting in flushing and congestion of the skin and increased

of an individual's skin, especially as concerns the pilosebaceous apparatus. This is illustrated by the present case.

## REPORT OF A CASE

A third class petty officer in the U S Naval Reserve, aged 18, was returned to the United States after approximately four months at an advanced base in the



Fig 1—The lesions on the left side of the chin are pigmented nevi

perspiration apparently favor its development. Changes in diet, neglect or inability to keep skin and clothing clean, emotional disturbances and many other factors are also doubtless important in individual cases.

Most important of all, however, in the causation of acne vulgaris is the inherent character

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Southwest Pacific. As an incidental finding on arrival here it was noted that he had a localized eruption on the right side of the chest. The patient had been aware of a light brown pigmentation from his earliest childhood but no other eruption had been noted in this area, nor had he had acne vulgaris previously. The new lesions had appeared shortly after arrival in the tropics.

The eruption consisted of comedos and a typical papular and papulopustular acne vulgaris occurring in a nevus characterized by increased pigmentation and hypertrophy of the pilosebaceous apparatus. There were no acne lesions elsewhere except a few comedos and small papular lesions on the chin. The eruption promptly improved following his return to this country, leaving only the original nevus.

# EFFECT OF ENDOCRINE SUBSTANCES ON THE ADULT HUMAN SCALP

HUGO R RONY, M D  
AND  
SAMUEL J ZAKON, M D  
CHICAGO

In a previous communication<sup>1</sup> we presented evidence to show that injections of testosterone propionate given over a short period produce an increase in the number and the size of the sebaceous glands of the pubertal region in boys of prepubertal age. This report deals with the effect of testosterone and diethylstilbestrol on the scalps of adult males.

## METHOD

Two men were selected for this study. Subject A was 18 years old, with beginning premature alopecia, having lost about 20 per cent of his scalp hair during the previous year. He was under our observation for seven consecutive months and received the following treatment: (a) 40 mg of methyl testosterone daily by mouth for the first three months, (b) no treatment during the month that followed, and (c) 5 mg of diethylstilbestrol daily by mouth for the last three months.

Subject B was 34 years old and had a malignant alopecia areata for the past three years. About 90 per cent of the scalp was completely bald, eyelids and extremities were entirely devoid of hair and eyebrows, face, upper lip, chin and chest contained a few scattered hairs, the pubic hair was scant, but axillary hair was almost normal in amount. Physical examination and metabolism tests revealed nothing significant. He was under our observation for five consecutive months receiving (a) 40 mg of methyl testosterone daily by mouth and 25 mg of testosterone propionate twice a week intramuscularly for four months and (b) 5 mg of diethylstilbestrol daily by mouth during the month that followed.

In both patients small portions from the occipital region of the scalp were removed for histologic study with the use of a biopsy punch before treatment and at the end of each treatment period.

From the Department of Endocrinology, service of Dr H Isaacs, and the Department of Dermatology, service of Dr S J Zakon, Mount Sinai Hospital.

The androgen preparations used in this study were supplied through the courtesy of Roche-Organon, Inc., Nutley, N J.

<sup>1</sup> Rony, H R., and Zakon, S J. Effect of Androgen on the Sebaceous Glands of the Human Skin, Arch Dermat & Syph 48 601 (Dec) 1943.

## RESULTS

In subject A, increase in the amount of body hair was apparent during the period of testosterone therapy, and the scalp hair, which was dry, became noticeably oily. He believed that he lost less scalp hair during this period than before, but we could observe no noticeable regrowth of scalp hair. Histologic sections show decided increase in the number and size of the sebaceous glands in the scalp during this period (figs 1 and 2), which change was not wholly maintained a month after use of testosterone was discontinued (fig 3). During the period of administration of diethylstilbestrol, the mammary glands in the breasts responded with enlargement and with hyperpigmentation and hypersensitiveness of the nipples. On inspection no effects were noticed on the growth of scalp hair, and in the histologic sections the sebaceous glands were seen to have reverted to their original appearance (fig 4).

Subject B reported itching of the scalp during the period of testosterone therapy. Some new lanugo hairs appeared on the spots that showed hair before treatment and also on some portions of the scalp that were previously completely bald, however, the total effect was practically negligible. The preliminary histologic sections show large sebaceous glands characteristic of alopecia areata (fig 5), and there was further hyperplasia at the end of the period of administration of testosterone (fig 6). During the period of therapy with diethylstilbestrol, there was a decided loss of scalp hair and other hair, and the patient refused to continue longer to take that estrogen. Histologic sections indicate definite atrophic effect on the sebaceous glands after ingestion of diethylstilbestrol.

## COMMENT

Our finding that androgen has a stimulating effect on the sebaceous glands of the scalp in



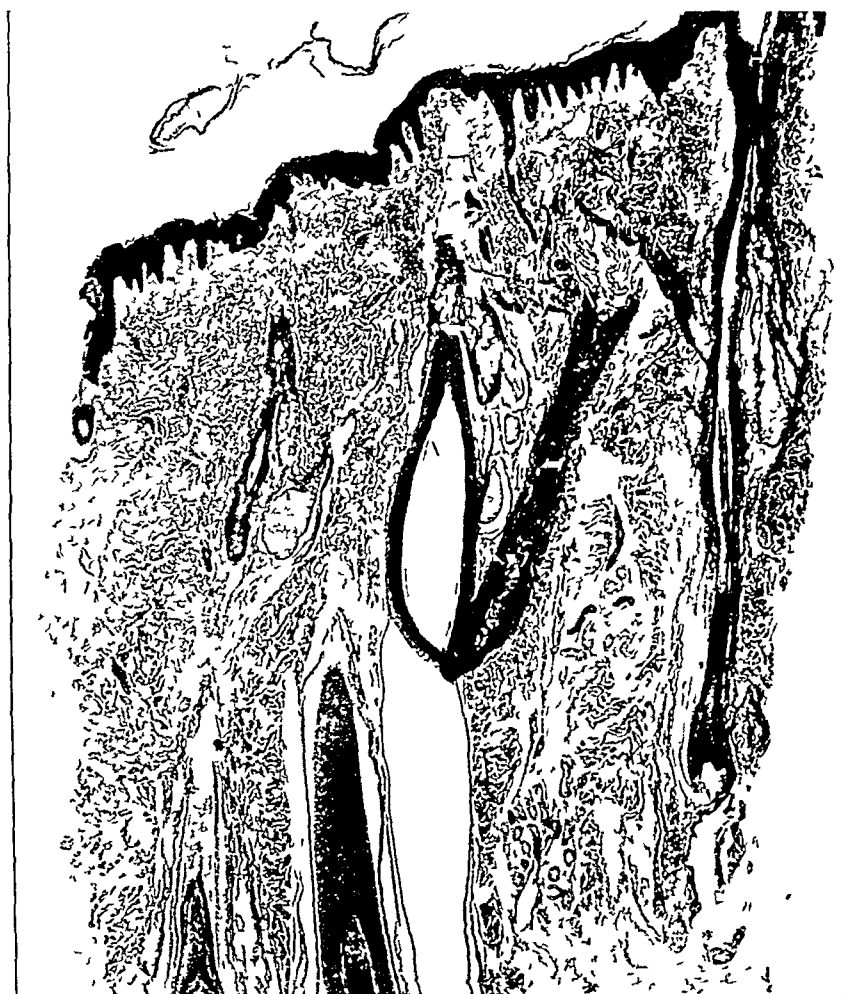


Fig 1—Section preliminary to treatment



Fig 2—Increase in the number and in the size of the sebaceous glands after methyltestosterone therapy

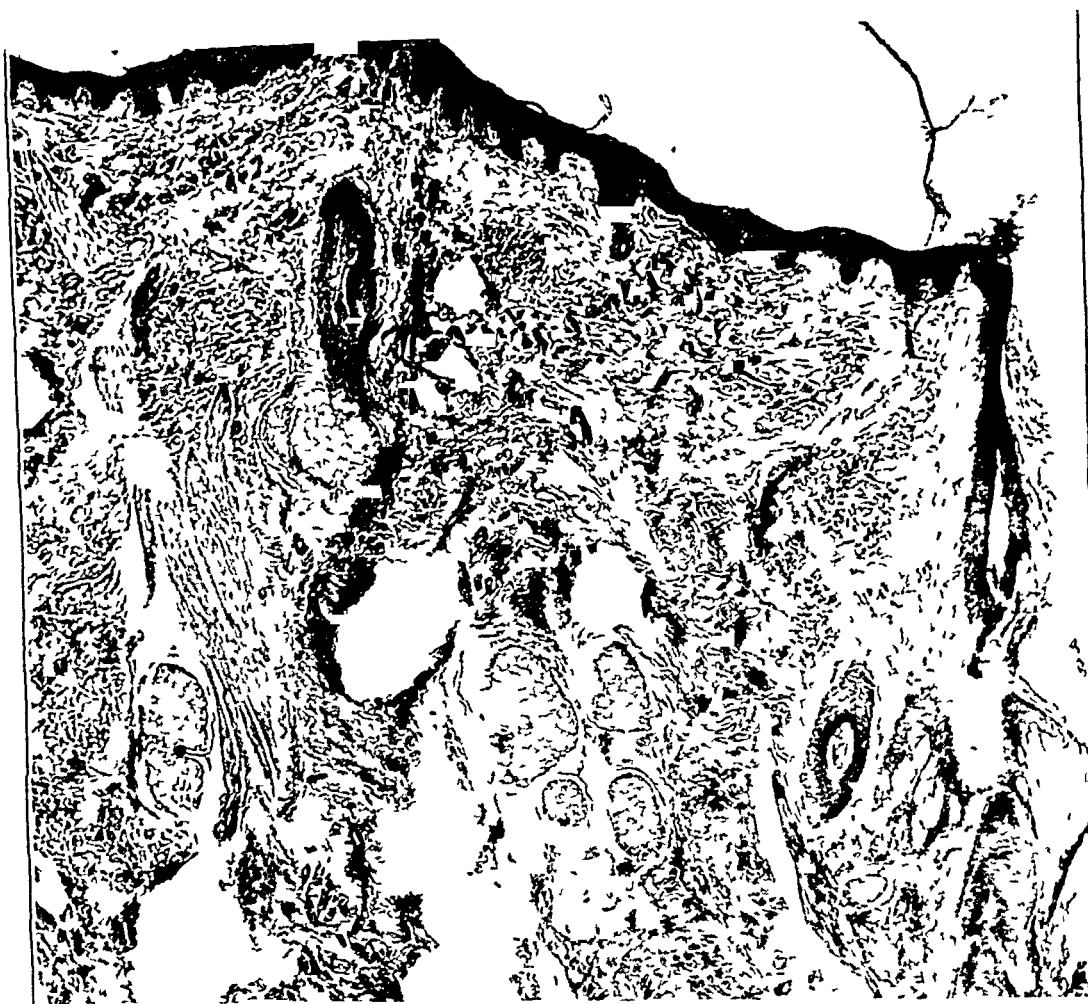


Fig 3—Decrease in the size of the sebaceous glands one month after methyltestosterone therapy was discontinued

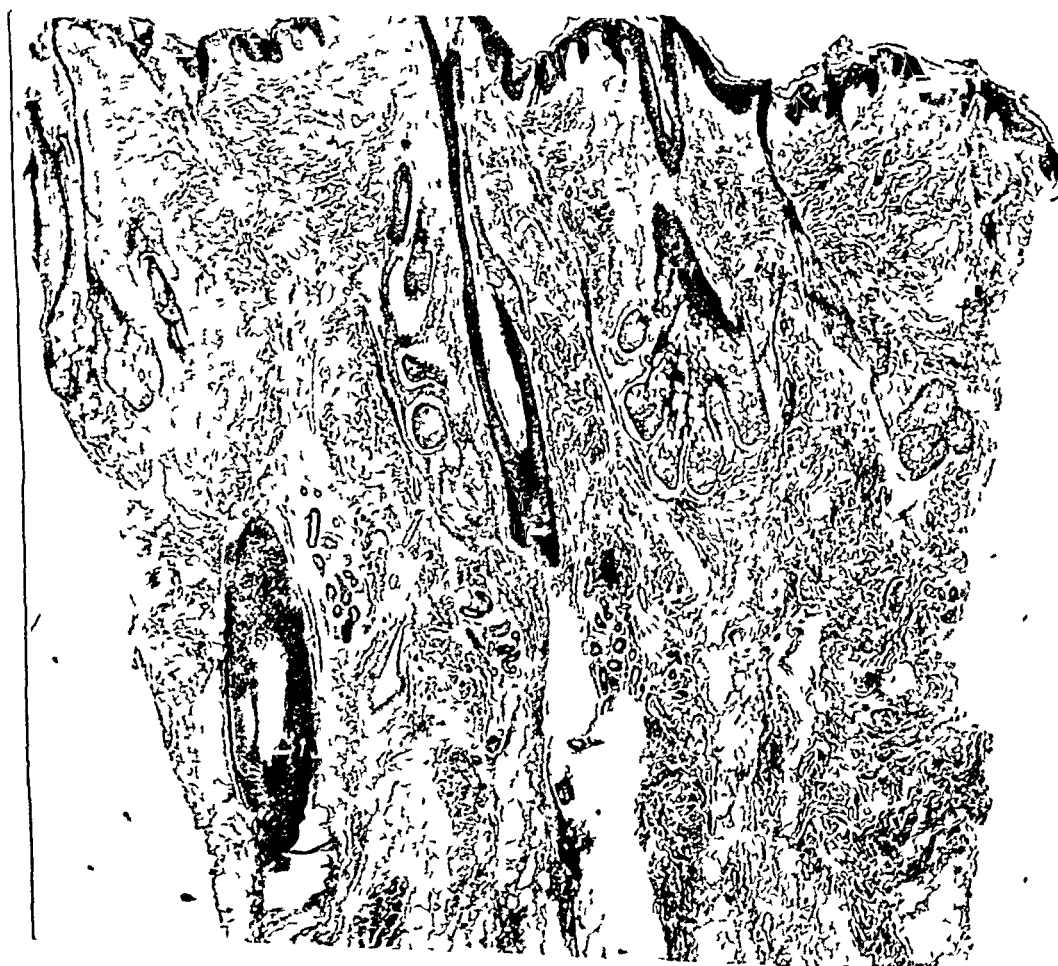


Fig 4—Reversion of hypertrophic sebaceous glands to original state after diethylstilbestrol therapy Compare with figure 1

these adults (as well as on those of the pubertal region in prepubertal boys) indicates that stimulation of the sebaceous glands is a general effect of androgen, regardless of the location of these glands or the age of the subject. It is of interest to note that this effect is powerful enough to produce further growth of the already hyperplastic sebaceous glands of alopecia areata.

Our further finding that diethylstilbestrol causes reduction in size and number of the

while stimulating the sebaceous glands in the scalp and the growth of body hair, did not promote the growth of scalp hair. This seems to indicate that the responses provoked by androgen in the hair follicles and in the sebaceous glands are two distinct and different phenomena: one phenomenon depends on factors of regional character, inherent in the responding tissue; the other phenomenon seems to be independent of such factors.



Fig. 5—Section of alopecia areata prior to any therapy

sebaceous glands in the human scalp is in agreement with Hooker and Pfeiffer's report<sup>2</sup> that the sebaceous glands of estrogen-treated rats become much reduced in size.

Attention is called to our observation that in the case of premature alopecia, testosterone,

<sup>2</sup> Hooker, C. W., and Pfeiffer, C. A. Effect of Sex Hormones upon Body Growth, Skin, Hair and Sebaceous Glands in the Rat, *Endocrinology* 32: 69 (Jan.) 1943.

#### CONCLUSIONS

The androgen methyl testosterone has a definite stimulating effect on the sebaceous glands of the adult male as well as of the male of prepubertal age. The estrogen diethylstilbestrol has a depressing effect on the sebaceous glands of the adult male.

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1 North Pulaski Road

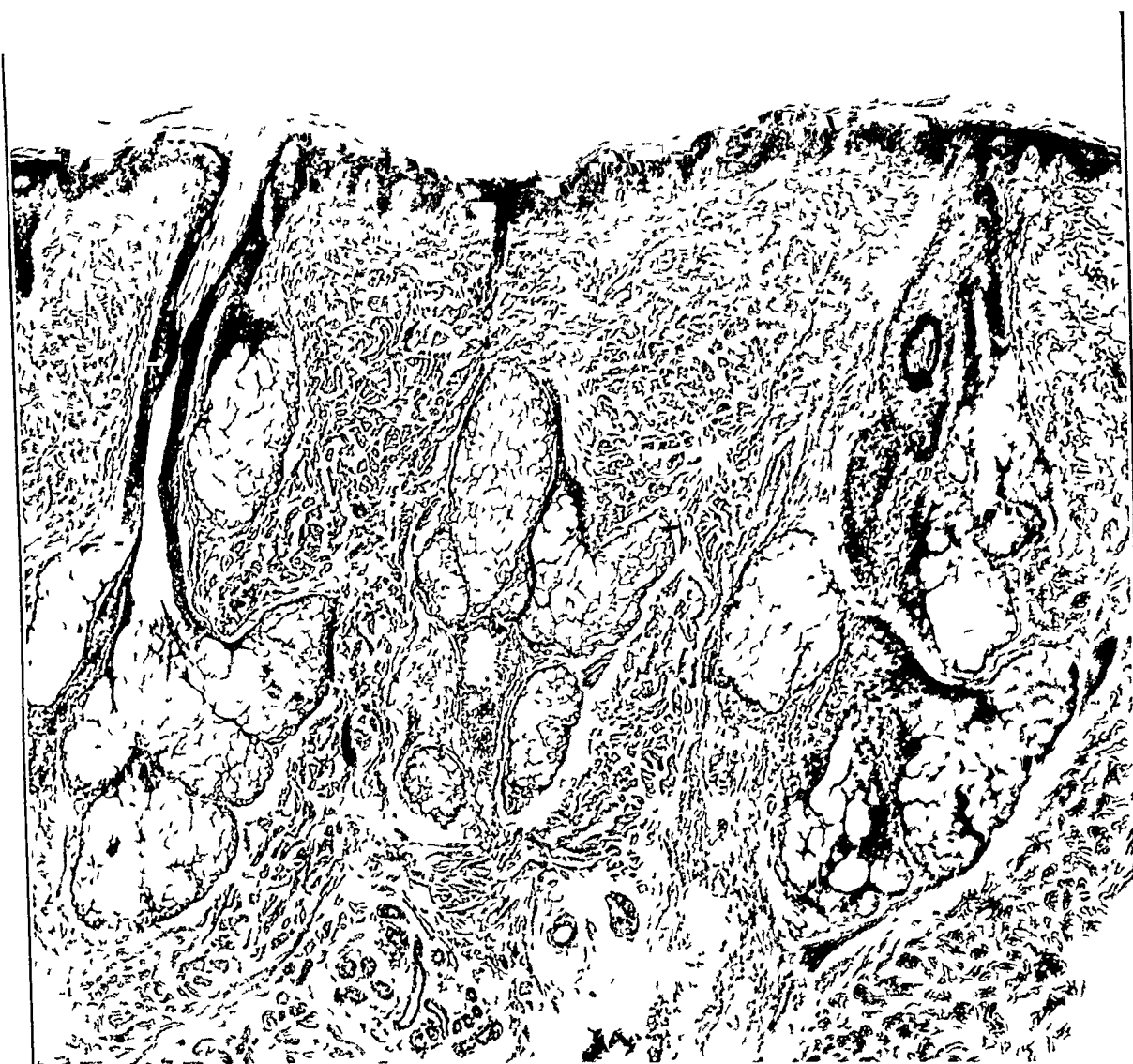


Fig 6—Decided hyperplasia of the sebaceous glands after methyltestosterone therapy

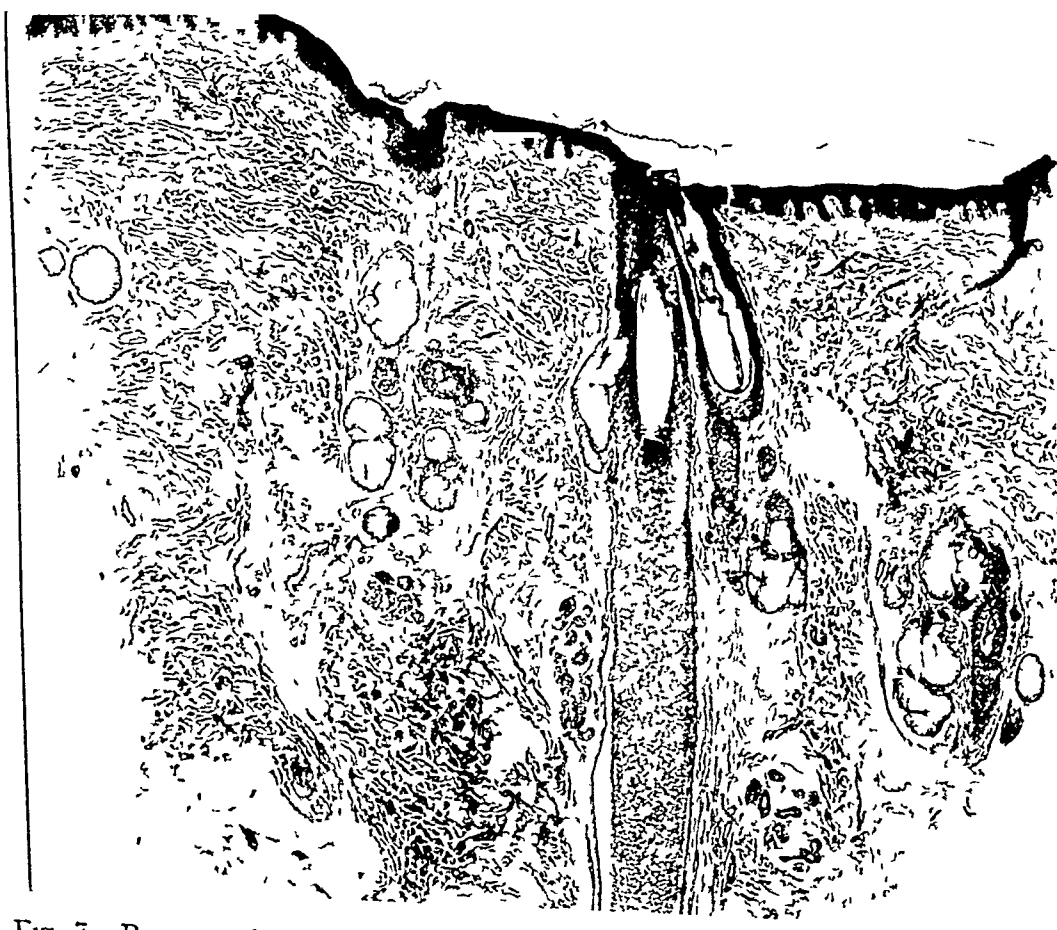


Fig 7—Pronounced atrophy of the sebaceous glands after diethylstilbestrol therapy

# EPIDERMODYSPLASIA HYSTRICOIDIS BULLOSA

## REPORT OF A CASE WITH HISTOPATHOLOGIC STUDY

JOSÉ G REYES, M D

NEW YORK

Under the name of epidermodysplasia hystricoidis bullosa a rare form of a congenital ectodermal malformation is here reported. The patient has been under my observation for more than one year, during which time a thorough study of the clinical symptoms and the histologic features of his disease has led me to the belief, after an exhaustive study of the literature on the subject, that this is so rare a disease that it has never before been reported.

### REPORT OF CASE

The patient is an 18 year old native-born Puerto Rican, who came to this country two years ago. He weighs 91½ pounds (41.5 Kg) and is 5 feet 3 inches (160 cm) tall. While he is not mentally deficient, he is slow to grasp ideas, his behavior is normal, and he is conscious of his eruption.

*Family and Personal History*—The mother claims to be well and in good health. She states that her husband died suddenly in 1938, of unknown cause. So far as she knows, no disease of the skin has been present in the family on either side, the boy being the only member of the family with such an ailment. She has had ten children, of whom three have died, and she states that all the children with the exception of J R (the patient), who was the eighth child, were normal in every respect. Of those living six are male and one female.

During the period of gestation with J R she felt a "kind of itch inside the womb" from the third month on, and, in order to obtain relief, she pressed and kneaded her abdominal wall. In addition to this unusual symptom she suffered from "morning sickness," which condition was also present during her other pregnancies, however, the "itch inside the womb" was present only during the pregnancy with J R. The mother also relates that during this time she noticed a craving for hot peppers with practically every kind of food she took and that the onset of this longing was from the very beginning of the gestatory period. This yearning was not experienced during any of the other pregnancies.

At full term and after an uneventful period of gestation the child was born. The mother was in labor for five days, had excruciating pains and discharged large amounts of amniotic fluid. When the child was born, the mother noticed that he was entirely covered with a "starch-glue-like substance" which would not come off when washed with soap and water. She related that during his first three years of life J R was constantly having trouble with his skin in the form of "blisters," which broke open easily, leaving an exposed and raw surface. After the third year he improved, with only small areas being affected, the process beginning, as usual, with the formation of "blisters."

At birth the hair of the scalp was a solid mass of interwoven hairs and crusts, the projecting ends had to be cut off with heavy scissors, owing to their barklike hardness. However, there was an area of baldness on the anterior part of the scalp. When the boy was 12, the hair began to improve in growth, consistency and distribution, and now that he is 18 the hair is normal, as is also the hair of the eyebrows, the eyelashes, the pubic area and the dorsal surfaces of the proximal phalanges of the hands and feet, where it is found in scantier quantity than is usual in boys of his age. A slight down is now beginning to appear on the upper lip.

*Symptoms*—The patient has a congenital patch of partial alopecia on the scalp, situated at about the left frontoparietal suture. It is half the size of a palm and is irregularly shaped, and its dry surface is covered with ichthyotic elements in the form of variously sized plaques. A few hairs, normal in every respect, are scattered in this patch. I believe that there must be a constant pruritic factor in this lesion, because every time I have examined it fresh scratch marks have been found, although the patient has never complained of pruritus. This area of alopecia is usually not visible because he combs his hair back, thus covering it. However, when the hair is streaming down over his face, it is noticeable.

The remaining part of the scalp seems to be normal except for the presence of fine furfuraceous slightly greasy white and gray scales in abundance.

The face used to be covered with crusts of various sizes and forms, but when the patient was 3 years old it began to clear. Now the skin of the face and ears looks dry and is covered with small flaky scales, similar to those following ultraviolet irradiation but without the erythema. The face is free from crusts, but the ears are covered with a few pea-sized flat crusts. The color of the skin of the face and the ears is dark, typical of the people of his race.

His physiognomy is somewhat peculiar, although there is no prominent frontal bulge and no depression at the base of the nose.

The teeth are irregular in shape. The upper incisors are normally set, while the lower ones are widely separated, especially the middle ones, which form a V-shaped gap with the angle pointing toward the gums. The other teeth approach the conical type.

The mucous membrane of the mouth, tongue, lips, palate and nose is normal and free from any lesion. The same can be said of the conjunctivas.

The skin as a whole is dry, dark and harsh, and it is covered with scales and horny hypertrophic elevations which vary in size, shape and thickness. The skin around the elbows and knees is extremely thick and looks like the bark of a tree.

In general the lesions are multiform, but there are four predominating types: (1) slightly elevated quadrilateral plaques, somewhat darker than the neighboring skin, with rounded margins which gradually merge with the neighboring skin, located on the upper part of the

dorsa of both hands, the wrists, the lower third of the extensor surfaces of the forearms and both thighs, the largest of the lesions being about 1 cm in diameter, (2) dark greenish elevated (about 2 mm) cuboidal lesions, with perpendicular sides and a smooth top surface, located in the intermammary region and separated from each other by deep furrows, (3) slightly dark ele-

are exaggerated and, in some areas, are covered with slightly raised grayish black crusts, producing rectangular and quadrilateral lesions, similar to those of lichen simplex chronicus of Vidal

The lesions found in the supraclavicular areas are slightly more raised than those in the infraclavicular areas. The left clavicle is bulky and bulges forward,



Fig 1—A, cuboidal lesions (darker part) of the hystrix type, on the chest, B, patch of congenital partial alopecia, C, plaques and the ichthyosiform features (Note the ruptured bulla on the dorsum of the right hand at the third metacarpophalangeal articulation)

vated (about 2 mm) polygonal or round verrucous lesions, located in both inguinal regions and separated from each other by deep furrows, and (4) bullae, which are usually tense and contain a clear fluid, that are produced by external injury

These lesions have the following distribution. The skin of the neck is dry and wrinkled, its normal lines

particularly at its junction with the sternum. The right clavicle seems to be normal.

The shoulders, axillae, axillary folds, upper extremities, chest, back, abdomen, flanks, inguinal areas and lower extremities are covered with variously sized and shaped lesions (oval, round or polygonal, cuboidal and quadrilateral), which are elevated from 1 to 3 mm



above the *muveau*. Both the flexor and the extensor surfaces of the extremities are involved, as well as the cubital and popliteal flexures.

The lesions are closely set around the nipples and in the intermammary and pectoral areas. Those on the back are closely packed, especially on the upper part and along the line formed by the spinous processes of the vertebral column. The lesions on the nipples and around them, when closely viewed, give to the nipples the appearance of artichokes, they are almost black, especially at the very tips, and the central lesions attain an elevation of about 3 mm. The lesions of the intermammary area are cuboidal, flat topped and gray-green, they are separated by furrows and are raised about 2 mm, giving the appearance of gray-green stale dough cracked open by drying. The lesions below the pectoral areas and on the flanks follow the lines of cleavage of the skin and are small, verrucous and crusted, forming broken ridges running transversely to the axis of the body. The lesions on the abdomen are of the same type. Those on the lower part of the abdomen and in both inguinal areas take the form of thick broken lines, separated by furrows which follow the lines of cleavage of the skin. Those in the inguinal areas are of the polygonal or round verrucous type, raised about 2 mm above the surface of the skin, and are of a dirty gray color. Some crusts of the flat type are noticed on the scrotum, the penis and the prepuce.

The area where the belt produces friction is more or less free of lesions. The sacroiliac and sacral regions are almost free of lesions of any type, and here the skin looks normal, a few healthy hairs being scattered throughout these areas. The normal creasings of the natal folds are exaggerated in the form of slightly raised ridges, which have a semicircular arrangement.

On the arms the lesions are oval, round or quadrilateral plaques, the last being the most predominant type, and are more numerous on the posteromesial aspects. These lesions are raised about 1 mm from the surface of the skin, and the largest are found around the elbows, where they produce tremendous thickening and wrinkling.

On the forearms there are flat raised plaques, covering both the extensor and the flexor surfaces. The lesions on the extensor surfaces are larger and thicker and are elevated about 2 mm, while those on the flexor surfaces are raised only about 1 mm. The predominant lesions on the lower third of the forearms are of the quadrilateral type, which lesions are also found, but more pronounced, on the dorsal aspects of both wrists and the upper half of the dorsa of both hands. The lesions on the lower half of the dorsa of both hands and the dorsal aspects of the fingers are larger but less raised than those on the wrists. The skin of the dorsal surfaces of the terminal phalanges is thick and is covered with few crusts. The finger nails and the palms are normal.

The extensor, flexor, medial and lateral aspects of the lower extremities are covered with flat lesions of various sizes. However, those on the extensor surfaces are larger and more pronounced than those found on the backs of the thighs. The lesions of the popliteal areas appear in the form of broken elevated ridges following the normal creases of the skin and are similar in form to those found on the lower part of the abdomen and in the natal and axillary folds. The creases around the knees, especially in the patellar areas, are grotesque and largely exaggerated, and this skin when grasped between the fingers gives a barklike sensation to the touch. The muscles of the lower third of the right thigh are more

highly developed than the corresponding ones on the other thigh, probably because of the patient's slightly irregular gait.

The lesions on the legs are flat, squamous and exfoliating and lie almost even with the skin, however, the lesions on the gastrocnemial areas are larger and more raised. Normal hairs are found here and there on the thighs and legs.

The lesions around the ankles are also flat, the skin is thickened, and its normal creasings are exaggerated.

The lesions on the dorsa of both feet are flat and squamous and are separated by fine furrows. The skin on the dorsal aspects of the toes is normal save for an occasional exfoliating scale here and there. The soles and toe nails are normal.

Since birth the patient has had vesicles and bullae appear on any portion of the body subjected to trauma, friction or injury. The same still is true now that he is 18. These bullae are tense and contain a clear fluid, which microscopically showed leukocytes and degenerated prickle cells. They rupture easily, leaving a smooth pink surface, which later becomes pigmented and finally becomes verrucous or ichthyotic. Some bullae, however, become secondarily infected, this complication is troublesome and demands attention, because the infection may easily spread to the neighboring areas. Thus, recently, the patient came to my office with a bullous lesion the size of a grape. It was located on the dorsal aspect of the second metacarpophalangeal articulation of the left hand and had been produced by a glancing blow. Its fluid was clear. Two days later the lesion ruptured, showing a pinkish and smooth area, which looked dry. The exposed areas are extremely sensitive, especially when they come in contact with water.

None of the mucous membranes have ever been affected by either vesicles or bullae.

Despite the presence of bullae, milia—either grouped or solitary—are typically absent.

The patient has an odor which at close range is offensive.

I have seen the patient perspire freely during the summer months, thus indicating that his sweat glands are normal and active.

*Histologic Study*—A specimen for biopsy was sent to Dr. Fred D. Weidman, University of Pennsylvania, who submitted a detailed report from his histologic study, a summary of which is given here.

There was an extraordinarily thick layer of hyperkeratotic material (psoriasiform) overlying the surface of the skin except for one region in the center, here the changes were such as to indicate the presence of excoriation. The keratinous substance was arranged in irregular lamellas, but, unlike those of psoriasis, they were extremely wavy and not sharply demarcated. Their wavy contour corresponded more or less to that of the epidermis underneath. It was clear that the surface of the epidermis was thrown up in low verrucous projections.

The stratum granulosum was also excessively thickened, in places it constituted fully half of the epidermis. It was vacuolated to such a degree that it could take on a reticulated pattern, with the cytoplasm of the cells disposed on a general region of edema which was traversed by strandlike remnants of the cytoplasm. In short, the picture was that of spongiosis but translated and largely confined to the uppermost regions of the epidermis. This spongiosis continued in places into the prickle cell layer but not into the stratum germinativum. Keratohyaline granules were abundant.



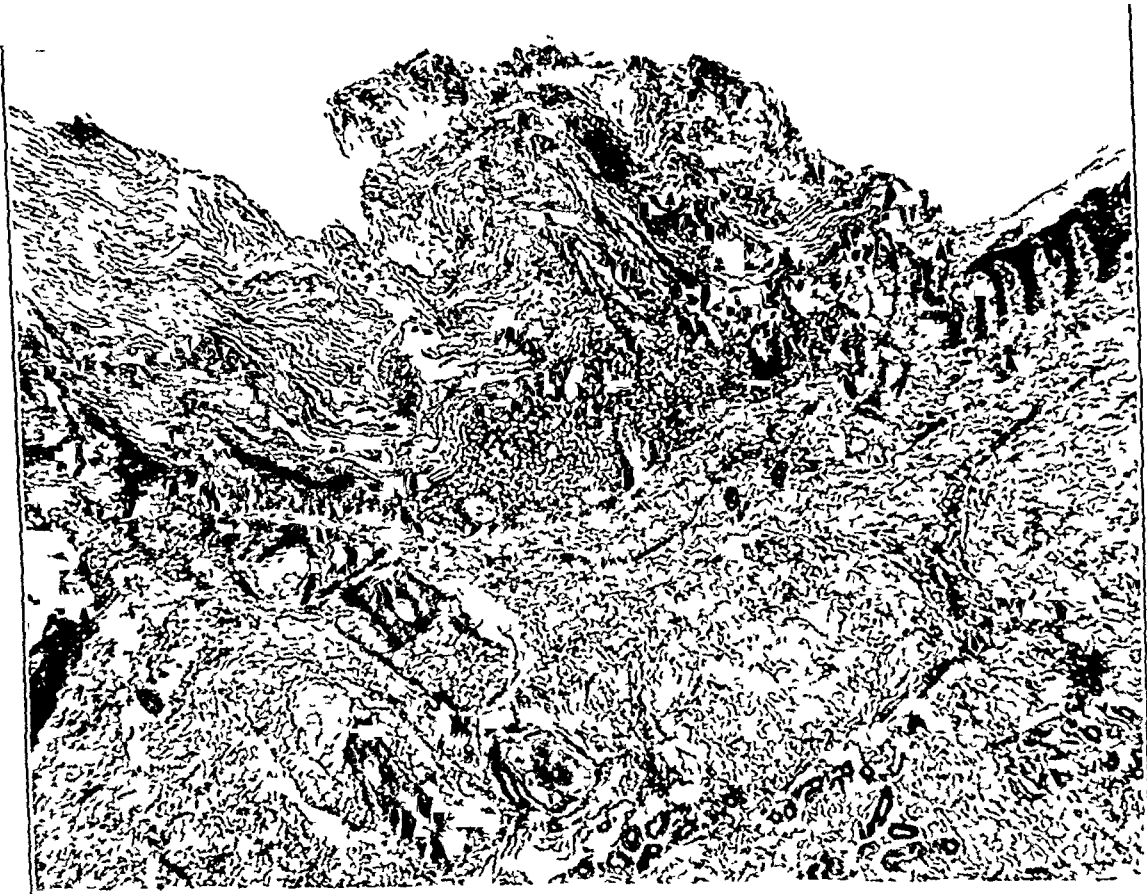


Fig 2—Low power view illustrating the extreme grade of hyperkeratosis and the degree of epidermal change underneath it by contrast with normal epidermis at either end of the section. Note that the thickening of the skin is accounted for mostly by changes in the upper parts of the epidermis.

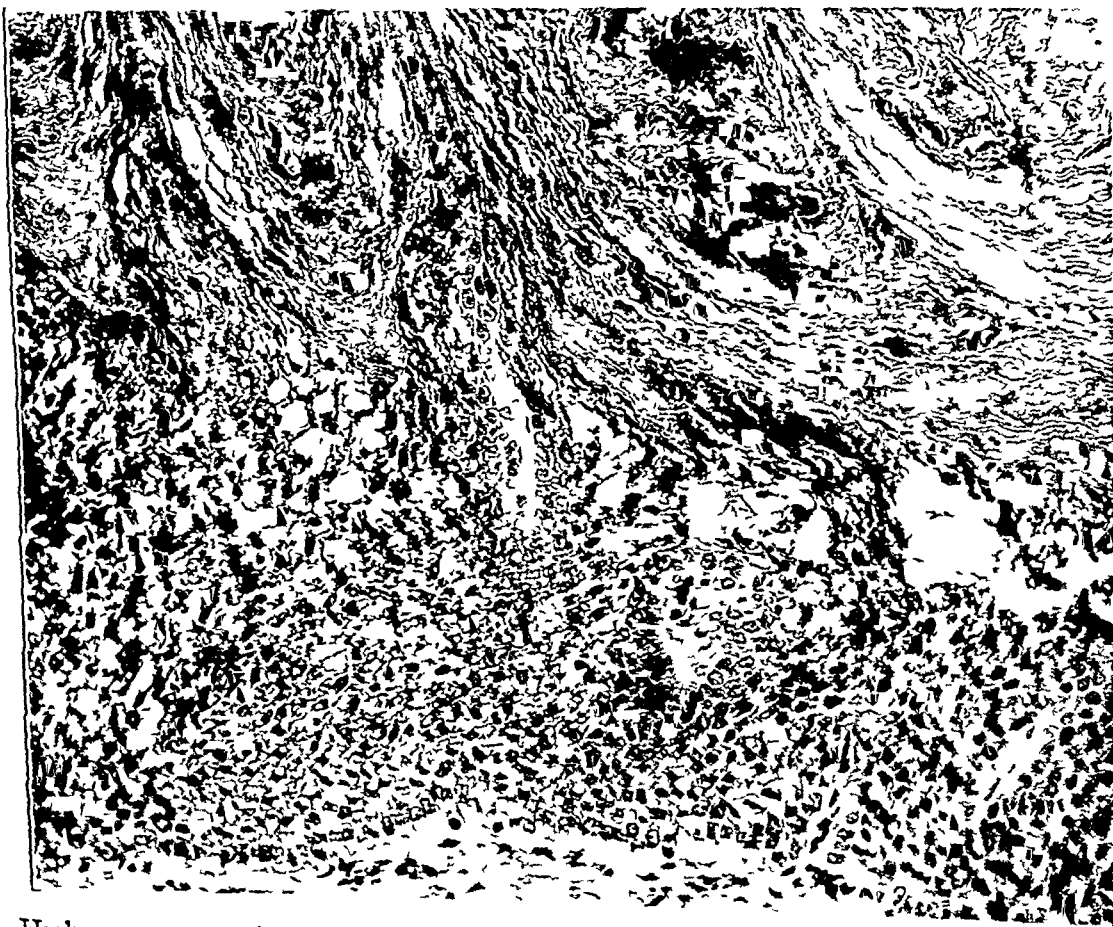


Fig 3—High power view showing a portion of the epidermis. In addition to the hyperkeratosis at the top of the photomicrograph, the details of epidermal change are demonstrated. The stratum granulosum is predominantly affected, thickened, increased in granule content and vacuolated.

The interpapillary pegs varied in length and shape but in general were not greatly elongated by any means or notably deformed. If anything, the epidermis was thin as regards the more viable parts in the stratum germinativum and spinosum. This fact indicates that the process was not fundamentally hyperplastic, the thickness of the epidermis was the result of abnormalities in the stratum granulosum together with their consequent product, keratin. In short, it was an abnormality of keratinization.

In the corium there were no important changes. The papillae were normal except for deformity consequent on whatever irregularity there was in the interpapillary pegs. Around the blood vessels there was but a minor grade of edema and lymphocytic infiltration.

The pilosebaceous apparatus and sweat glands were numerous, highly developed and apparently normal. Perhaps the sebaceous glands were hypertrophic, and the same may have been true for the sweat glands. This statement cannot be made positively without a study of control specimens from normal ipsilateral positions.

As confirmed by sections stained by Weigert's method, elastic tissue was entirely absent in the uppermost parts of the skin. Farther down it was present in small quantities, and such as there was was grouped into local aggregations and was highly fragmented.

In summarizing and interpreting Dr. Weidman's observations it becomes apparent that the scarcity of elastic tissue was consistent with epidermolysis bullosa. The fact that pathologic changes were almost entirely in the stratum granulosum and stratum corneum was consistent, too, with ichthyosis. The thickness of both of these layers was striking, as was the form which the changes in the stratum granulosum had taken.

*Laboratory Observations*—The chemical examination of the blood showed blood sugar 83.3 mg per hundred cubic centimeters, urea nitrogen 16.9 mg, nonprotein nitrogen 35.15 mg, uric acid 2.3 mg, cholesterol 120 mg and calcium 10 mg.

The urine was yellow and clear, with no sediment and was acid in reaction, with urinous odor. The specific gravity was 1.026, and total solids measured 5.7 per cent. There was no blood, albumin, diacetic acid, bile, dextrose or acetone detectable in the urine. The indican content was normal. The urea content measured 1.8 per cent of the volume. The microscopic examination did not show mucous threads, pus cells, epithelial cells, red blood cells, cylindroids, casts, phosphates, uric acid or calcium oxalate. Only a few amorphous urates were found.

The basal metabolic rate was subnormal, the Wassermann reaction of the blood was negative.

#### GENERAL CONSIDERATIONS

*Differential Diagnosis*—Epidermodysplasia hystricoidis bullosa has to be differentiated from other diseases due to anomalous formation of the ectoderm.

1. Ichthyosis, which, according to Darier,<sup>1</sup> "is never congenital but which manifests itself at an early age," must be ruled out. In my patient the disease is congenital. In a patient with ichthyosis the palms and soles are usually dry

and wrinkled, while in my patient they are normal. In ichthyosis the cubital flexures, the popliteal areas, the groins, the articular and axillary folds and the genitalia are almost normal, while in epidermodysplasia hystricoidis bullosa all these areas are covered with lesions of various types. In ichthyosis the sweat and sebaceous secretions are notably diminished in contradistinction to the increases observed in my case. Ichthyosis is usually aggravated by cold weather, but my patient's disease has improved during the winter months. In ichthyosis the hair becomes dry and the nails brittle, breaking easily, this is in contrast to the condition seen in my case.

2. In patients with epidermolysis bullosa one finds single or grouped milia, which are entirely absent in my patient. In cases of epidermolysis bullosa the bullae are sometimes hemorrhagic, while in my case this has never been observed. In epidermolysis bullosa, the nails may show dystrophic changes and the mucous membranes of the mouth and tongue may be affected with bullae or patches of leukoplakia, while in epidermodysplasia hystricoidis bullosa they are normal. In patients with epidermolysis bullosa the healing of the bullae may be followed by scarring, but this has never been noticed in my patient, and, last, patients with epidermolysis bullosa reveal a significant hereditary or familial history, which my patient does not have.

3. In patients with pachyonychia congenita of Jadassohn<sup>2</sup> the nails are thickened, folded longitudinally, opaque and lusterless. There are also palmar and plantar hyperkeratoses, anomalies of the hair and leukoplakia. Verrucous lesions occur on the elbows, knees, popliteal regions, buttocks, leg and ankles, with bullae occurring chiefly on the plantar surfaces. In my patient, the nails, palms and soles are normal, there is no leukoplakia, and the partial alopecia in the scalp is outstanding.

4. In cases of erythroderma ichthyosiforme congenitum there is a generalized erythroderma, which later in the patient's life may disappear, leaving an ichthyotic skin, the picture of the disease is that of ichthyosis plus redness. Unlike the distribution in my case, the flexor surfaces are the sites of predilection for this disease. The palms and soles, the buccal and nasal mucosae and the eyes are invaded to a variable degree, and the face is usually red. The bullae occur as a complication, appearing most fre-

<sup>1</sup> Darier, J. *Precis de dermatologie*, ed 4, Paris, Masson & Cie, 1928, p 254.

<sup>2</sup> Cited by Sutton, R. L., and Sutton, R. L., Jr. *Diseases of the Skin*, ed 10, St. Louis, C. V. Mosby Company, 1939, p 561.

quently on the extremities, and are of the flaccid type, disappearing without sequelae to reappear during the winter months. As a rule they disappear permanently when adult life is reached. Perspiration is limited except on the flexures of the extremities and on the palms and soles. In my case, again, there is a patch of partial alopecia in the scalp.

The histologic features of epidermodysplasia hystricoidis bullosa might suggest several other conditions in which it is known that the fundamental pathologic changes are those of an epidermodysplasia. All these, however, can be eliminated on clinical grounds, particularly because they are not ichthyosiform. Mention is made in this connection of only a few.

5 In nummular and confluent papillomatosis the lesions are verrucous nummular papules, with reddish reticulum. In 1 case the onset occurred when the patient was 13 years old, the intermammary area being affected first. The scalp was normal.

6 In verrucous papillomatosis (Gougerot, Clara and Bonnin<sup>3</sup>) the lesions are round raised brownish papules, elevated about 1 to 2 mm. The area first affected is the dorsa of the hands, then the wrists and the forearms and, later, such areas as the face, neck and palms. The volar surfaces and the scalp are not affected at all, and the onset is in adult life.

7 In epidermodysplasia verruciformis (Lutz and Lewandowsky<sup>4</sup>) the lesions are found all over the body in the form of plates, 1 to 2 cm in diameter, and pale red or reddish papules, which may be round, oval or polygonal, with straight margins, even surfaces and no trace of pigmentation. Grayish scales are also noted, which may be removed. The scalp is involved from early life. The lesions in this disease are present at birth.

8 In punctate papillomatosis (Gougerot and Clara<sup>5</sup>), the lesions are punctate verrucous papules, which affect the neck, the trunk and the extremities. There is also stippled erythema of the face and scalp and porokeratosis of the palms and soles. The onset of the disease in the case reported<sup>5</sup> occurred when the patient was 13 and the lateral parts of the body were affected, from whence it spread to other areas. The eruption disappeared during the months of autumn and winter. The seborrheic regions of the body were especially involved. On the scalp

and on the face there were crusts which when removed exposed small ulcers.

9 In confluent and reticulated papillomatosis the onset occurs between the fifteenth and twenty-sixth years of life. The lesions first appear in the intermammary area, where they take the form of verrucous papules, varying in size from 1 to 2 mm in diameter, and are a deep gray. As a rule, confluence occurs in such a way that reticulated areas are formed. The scalp remains normal.

*Prognosis* The prognosis as to life is good but as to cure is a moot point.

*Treatment* At present nothing definite can be said regarding treatment, inasmuch as no good results have been obtained from the external and internal medications used. Singularly, the patient states that he has been greatly benefited by the change of climate brought about when he came to New York from the tropics.

#### COMMENT

In substance, the changes previously described indicate that the pathologic processes are of two kinds. First, there is hyperkeratosis, both clinically and histologically evident. Microscopically, it takes the form that justifies the designation "epidermodysplasia", this is consistent, incidentally, with the characteristics exhibited in ichthyosis as well as in other entities. There is a circumstance additional to the picture typical of ichthyosis in that there is a patch of incomplete alopecia in the scalp, since it was congenital, it must be regarded as a part of the original pathologic processes and not secondary thereto. This being the case, it appears logical to explain the loss of hair on the basis that the abnormal keratinization included the hair papillae as well as the surface epithelium and led to disappearance of hair. It is granted that this theory is speculative, and it is submitted in the absence of any reasoning that is more appealing. I have no explanation why the nails, palms and soles did not participate in the abnormalities of keratinization.

The second kind of change is of the order of that which occurs in epidermolysis bullosa again, with respect both to clinical and to histologic phenomena (bullae, the traumatic factor and the scarcity of elastic tissue). In summary, in my patient there were two congenital shortcomings—one, concerning keratinization, and the other, concerning elastic tissue. Both of these shortcomings were demonstrated histologically, and thereafter the line of reasoning in relation to the clinical picture follows the conventional path of ichthyosis and epidermolysis bullosa.

<sup>3</sup> Cited by Sutton, R. L., and Sutton, R. L., Jr. *Diseases of the Skin*, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 870.

## SUMMARY AND CONCLUSIONS

The name chosen for this disease conforms to the clinical and histologic observations. It is a congenital ectodermal abnormality with characteristics of its own. Clinically, there are a congenital patch of partial alopecia in the scalp, a congenital ichthyotic skin and the exuberant warty excrescences of ichthyosis hystrix and bullae, which are produced by external irritation or trauma through a congenital factor and which heal without scarring. Histologically the disease is an epidermodysplasia, because the bulk of the pathologic changes are located in the upper layers of the skin, as in ichthyosis, the main pathologic features occur almost entirely in the stratum granulosum and the stratum corneum. Moreover, as in epidermolysis bullosa, there is a congenital loss of elastic tissue and, last, in connection with a congenital ichthyosiform dermatosis, cer-

tain additional features may appear, which cannot be reconciled with any of the existing dermatologic entities that are more or less ichthyosiform. The most important of these are (a) a patch of congenital partial alopecia of the scalp, (b) the absence of changes in the nails, mucous membranes, hair, palms and soles, (c) the occurrence of bullae in a congenital ichthyotic skin, and (d) the absence of milia.

Accordingly, it appears to be proper to apply a special term for the condition, namely, epidermodysplasia hystricoidis bullosa.

NOTE —After this paper was completed and was ready to be submitted, I encountered another case of epidermodysplasia hystricoidis bullosa at a local hospital. This patient was an American-born white youth of 18, whose disease was diagnosed as ichthyosis hystrix with vesiculations.

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# DERMATOLOGY IN AN ARMY STATION HOSPITAL SERVING IN ITALY

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MEDICAL CORPS, ARMY OF THE UNITED STATES

The relative position and functions of the dermatologic section in any hospital are generally the same as in any other, whether it be a department of a civilian hospital, of an army hospital in the continental United States or of an army hospital on overseas duty. One can reasonably expect, however, some variations and differences in the problems and procedures of dermatologic practice in hospitals of different nature, organization and geographic location.

An army hospital serving overseas usually has some limitations of equipment, supplies and personnel which hospitals in the Zone of the Interior do not as a rule have. Sanitary conditions under which soldiers have to live at the front, in bivouac areas and in replacement centers behind the lines may account for a higher number of bacterial and parasitic diseases of the skin than may be seen in hospitals in the United States. Parasites peculiar to a geographic area may cause a higher incidence of a particular type of parasitic diseases. The number of such diseases may be increased by the poor sanitary conditions of the civilian population with which soldiers come in contact, such as the populations of the zones of military operations and of war-torn cities and villages.

Under combat conditions, not only is the soldier exposed to infections but also facilities for early treatment may be lacking, so that when treatment can be obtained after some delay an otherwise banal cutaneous disease may be so aggravated that the soldier has to be hospitalized for an extended period. For instance, in many cases of scabies, the most simple medication cannot be carried out because of rough combat conditions. Such delay may result in a more or less severe pyoderma and makes hospitalization necessary for a disease which is routinely treated by battalion medical officers when handled under better living conditions.

Chronic cutaneous diseases which in favorable circumstances do not cause any discomfort may be aggravated by exposure to cold, strenuous marches and poor sanitary conditions. The mildest forms of psoriasis may send soldiers to the hospital after some time on the front line.

Soldiers with congenital ichthyosis who had never been hospitalized in civilian life or when stationed in the continental United States, may have to spend weeks in the hospital after the onset of cold weather, when exposure and lack of bathing increase their complaints. Soldiers in combat units, wearing woolen clothes all through the hot summer months and woolen underclothes in the winter, who previously were not accustomed to wearing wool for an extended period, may and often do get sensitive to wool, and acquire extensive contact dermatitis.

Under the stress and strain of war, neurodermatitis, both the disseminate and the lichen simplex chronicus (neurodermatitis conscripta) types, causes increased complaints and gets more attention from the patient's finger nails, securing him not only some pleasure and relief from emotional tensions but often an easy means to escape rough conditions and combat. On the other hand, owing to the general good health and the age of soldiers on overseas duty, some types of cutaneous disease are seen only rarely in hospitals serving front line troops, diseases which may be seen routinely by dermatologists practicing in civilian hospitals. Such dermatoses may be manifestations of the various allergies, contact dermatitis connected with civilian occupations, dermatoses affecting the younger and the aged groups or chronic and incapacitating diseases of the skin precluding military service.

Army dermatologic practice in a station hospital serving in Italy may show some differences from practice in other geographic areas, which may be of interest to dermatologists in civilian hospitals, army dermatologists in the Zone of the Interior or in other theaters of operations.

The hospital to which I have been assigned has been in operation on the Italian peninsula for over a year. Many station hospitals on overseas duty handle their dermatologic patients casually among the various medical admissions, owing to lack of trained personnel or to limited facilities. This hospital has a dermatologic section with facilities and personnel adequate to care for most types of dermatologic cases.

## THE DERMATOLOGIC SECTION

The dermatologic section of an army hospital is a subdivision of the medical service. While in some hospitals the dermatologic department cares also for the patients with venereal disease and often include patients with syphilis, in this hospital the dermatologic section excludes persons with venereal disease. Patients with syphilis, penile lesions, gonorrhea and lymphogranuloma venereum are treated in the urologic section, which is in charge of a urologist.

The dermatologic department has a sixty bed ward and an active outpatient clinic, located in a permanent building sufficiently repaired and altered to secure comfort for the patients. Between the two wings of the ward, a spacious office was built to serve as the administrative office, examination and treatment room and also as the outpatient clinic. A smaller compartment attached to it serves as a storeroom for medicines and dressing materials and also as the place for routine ward treatments dispensed by the nurse or trained technician. The nurse's desk and the patients' waiting room occupy the remaining space between the two ward wings. A diet kitchen, a storeroom for linen and two wash closets, each with one sink, are parts of the ward proper. Water is heated on oil heaters or on a small electric plate, according to the amount required. Electric lights and facilities for heating are adequate. Bathtubs, showers and latrines are located in another building of the hospital. This is slightly inconvenient in the management of the occasional seriously ill bed patient. Recently a bathtub has been installed in the ward.

The equipment consists of the simplest instruments for examination and treatment. The beds are partly steel hospital beds and partly folding field cots. Furniture such as bedside tables, benches, examination tables and desks is homemade with the help of patients and Italian labor. Routine laboratory work is done in the laboratory of the hospital. Biopsy specimens are sent to a general army laboratory stationed nearby. Roentgenologic treatments, diathermy and short wave diathermy are not available, but the physical therapy section has a good air-cooled ultraviolet lamp, which is used largely for the treatment of patients with cutaneous disease.

The personnel consists of an officer dermatologist in charge, two nurses and a sergeant wardmaster, all of whom are trained and skilled in nursing patients with cutaneous ailments.

A skilled noncommissioned officer serving as clinical assistant is in charge of the clerical details and the outpatient clinic. One or two ward-

men, more or less subject to change, and an Italian laborer make up the rest of the personnel.

While some morning hours are reserved for the outpatient clinic, the location of this clinic in the ward office makes it possible to see outpatients any hour of the day. Patients, who often come from great distances for consultations, do not make unnecessary trips on account of restricted hours. Suitable arrangements with the pharmacy and with the physical therapy section make it possible to see any patient, make a diagnosis, treat him and supply him with the necessary medicine, within a short time, so that he can return to duty without unnecessary loss of time. His return visits are kept at a minimum.

## SOURCES OF ADMISSION

Patients are admitted from a number of units, such as base section troops, service units, replacement centers and training and reconditioning units stationed within a certain area around the hospital. Soldiers are seen at the daily sick call by the unit medical officer, and if this officer thinks hospitalization is necessary he forwards them to the admitting office of the hospital. Otherwise, a great percentage of patients with routine dermatologic diagnoses are treated by the unit medical officers and are sent to the outpatient clinic of the hospital only if diagnoses should be difficult or treatment is unsuccessful. Most patients with scabies seen at the outpatient clinic are treated while on duty, only those in whom extensive secondary lesions and pyoderma develop are admitted to the hospital. The treatment of psoriasis is also managed on the outpatient basis, unless the lesions incapacitate the soldier to the extent that he cannot keep up with his regular duties. Most patients with pityriasis rosea are not admitted, but they visit the physical therapy section for ultraviolet treatments on one to six occasions. After the diagnosis has been made and a soldier is supplied with the necessary medicines and instructions, he is usually returned from the outpatient clinic to the care of the unit medical officer. However, in some cases treatment cannot be carried out successfully under the conditions in which the soldier has to live, and the unit medical officer returns the patient to the hospital for admission.

Other sources of admissions are the evacuation hospitals stationed immediately behind the front lines and the overflowing station or general hospitals.

Patients primarily admitted to this hospital for other than cutaneous diseases and having a concurrent complaint of a cutaneous nature are also seen at the outpatient clinic unless they



are strictly confined to bed. If their cutaneous disease outweighs their other medical or surgical ailments, they are transferred to the dermatologic ward.

Patients without cutaneous diseases are admitted to the dermatologic ward only if shortage of bed space in other general medical wards makes such a temporary measure necessary.

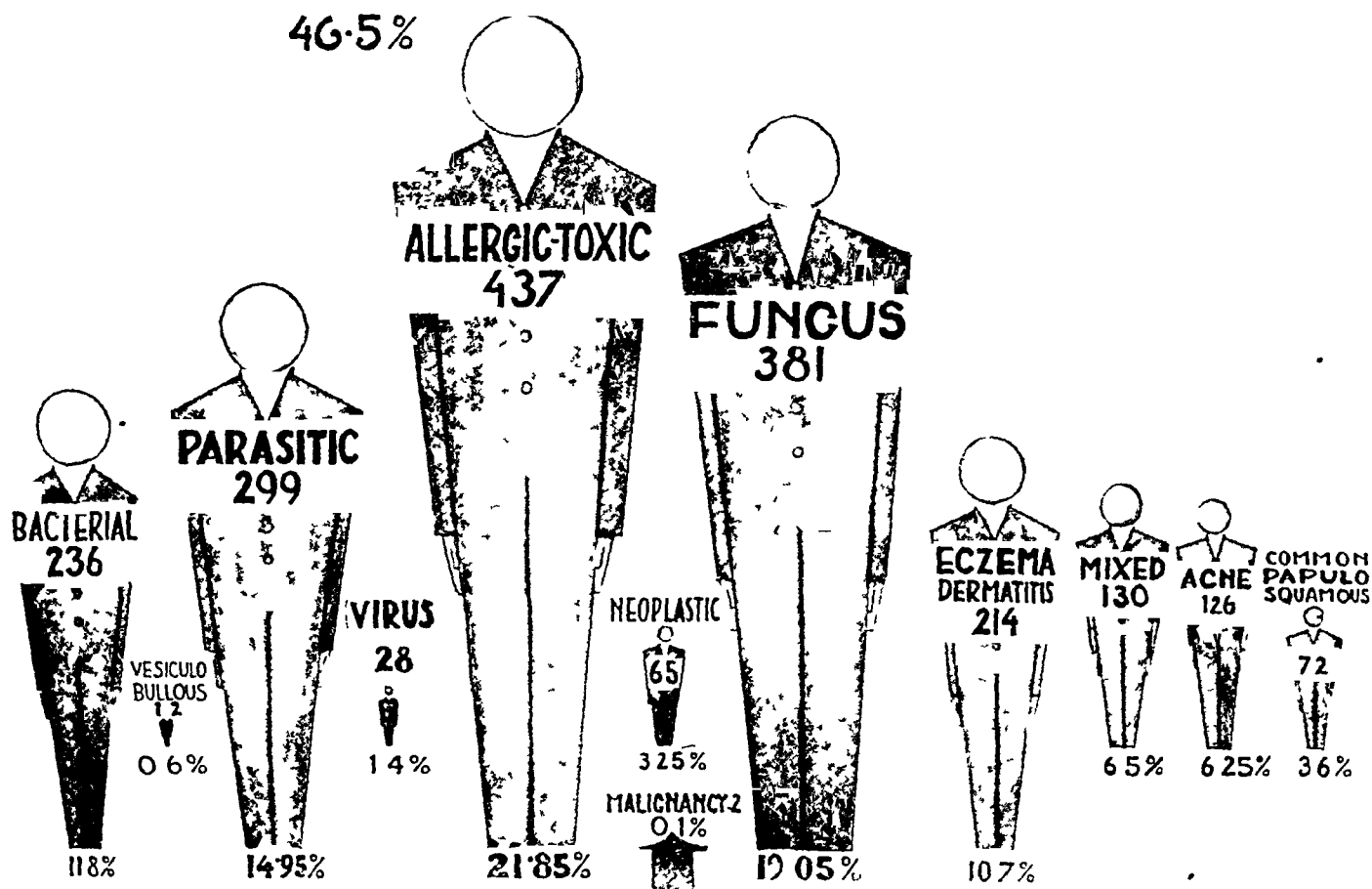
#### STATISTICAL DATA

In the first year of operation of this hospital of all patients hospitalized, 53 per cent were admitted on account of cutaneous diseases, excluding syphilis and penile lesions. This num-

cent of patients hospitalized in the station hospital at Fort Belvoir, Va., for dermatologic disease. The reason for the higher percentage in this overseas hospital may be a high percentage of cutaneous infections under combat and field conditions, under which a majority of soldiers overseas live. It may also be due to the lack of facilities for early treatment and to the consequent aggravation of otherwise harmless acute or chronic cutaneous diseases. Lack of adequate quarters and of hot water make the application of hot compresses impossible for a soldier whose home is a tent or a bomb-damaged house, and, although he may not be seriously affected, he

930

46.5%



Comparative sizes of the eleven diagnostic groups into which 2,000 dermatologic patients (930 [46.5 per cent] inpatients and 1,070 [53.5 per cent] outpatients) in an army station hospital in Italy were divided.

ber represents the percentage of patients treated for cutaneous conditions in the dermatologic ward. Some patients with furunculosis, ecthyma, cellulitis due to trichophytosis and other diseases were treated in the general medical or surgical wards and were not brought to the attention of the dermatologist. These are not included in the previously mentioned percentage. This is a considerably higher percentage than those published in reports from hospitals in the Zone of the Interior. Woolhandler<sup>1</sup> reported 2.6 per

cent must be hospitalized in order to carry out comparatively simple home treatments.

The yearly average hospital stay was nineteen and two tenths days. Patients were returned to duty as soon as their condition made it possible to carry them on ambulatory treatment by their unit medical officer, with occasional visits to the outpatient clinic of the hospital. One and three tenths per cent suffering from various chronic and partially disabling cutaneous diseases were boarded after improvement and discharged to limited service. Four and five tenths per cent of all patients suffered from cutaneous diseases necessitating a long period of hospitali-

<sup>1</sup> Woolhandler, H. W. Dermatology in an Army Station Hospital, Arch Dermat & Syph 49:91 (Feb) 1944.



zation or causing serious disabilities and were transferred to general hospitals for further treatment or evacuation to the Zone of the Interior

My colleagues and I have compiled statistical data on the first 2,000 dermatologic patients at this station hospital and analyzed and grouped them according to diagnoses. Of this number, 930 (46.5 per cent) were ward patients and 1,070 (53.5 per cent) were patients seen in the outpatient clinic. The ratio of hospitalized to clinic patients is also greatly at variance with the figure reported by Woolhandler.<sup>1</sup> He found in the Fort Belvoir Station Hospital that for each patient hospitalized there were 6.5 outpatients, whereas my ratio is 1:1.2. My ratio, therefore, is much closer to the figure reported by Pillsbury, Sulzberger and Livingood<sup>2</sup> from the Indiantown Gap Station Hospital, where the ratio of ward patients to outpatients was found to be 1:1.67. The number of average daily visits at the outpatient clinic of this hospital was 12, a figure corresponding closely to 14, that was reported by Woolhandler from the Fort Belvoir outpatient clinic.

We have analyzed the cases and placed our 2,000 patients in eleven diagnostic groups, using as a basis for this grouping the Pillsbury-Sulzberger Army "Manual of Dermatology."<sup>2</sup>

Our largest group, 437 patients (21.85 per cent), was comprised of the patients with allergic-toxic dermatoses. In this group we included all with allergic, contact and atopic cutaneous manifestations, urticaria, angioneurotic edema, dermatitis medicamentosa, dermatitis venenata, toxicoderma, erythroderma and erythema multiforme. The inclusion of persons with so many different entities may be the reason for this group's taking precedence over the next group, the patients with fungous infections, which in Woolhandler's report shows the highest percentage. Fungous infections were also the cause of the bulk of admissions for cutaneous diseases in hospitals of the Pacific theater, according to the communication of Ambler.<sup>3</sup> While it would be expected that one might see a large number of cases of dermatitis venenata caused by plants in most regions of overseas theaters, I have noted the rarity of such eruptions in our department. Woolhandler reported 68 cases of miliaria rubra among his 3,000 dermatologic cases. In our hospital, only a few cases of this disease were seen, undoubtedly not

on account of its rarity in this region, but rather because patients with this type of cutaneous disease were treated successfully at the battalion aid stations and were rarely seen at hospitals for consultations or treatments.

Our second largest group, 381 patients (19.05 per cent), was that of patients with the fungous diseases. We have noted the high incidence of fungous infections as secondary complications in the numerous cases of trench foot which came under my observation. Many patients in whom trench foot developed in the rainy or cold seasons contracted trichophytosis pedis either before they were admitted to the hospital or soon after their discharge. Some with apparently improved trench foot were doing well until the hot summer months when, after even short marches, they came down with severe trichophytosis pedis, suffering with continuous relapses thereafter even if they did not do extended marching or exercise. Hyperhidrosis, bromhidrosis, excessive pustulation, cellulitis, spreading of infection along the legs, contact dermatitis and resistance to treatment were other features of post-trench-foot trichophytosis. As relapses were common, demanding frequent hospitalization, we were hesitant to discharge these patients to duty before all signs of infection were completely cleared. Some of them had to be evacuated to the Zone of the Interior as unfit for general as well as for limited duty.

All fungous infections were of the superficial type, and we did not encounter any of the deep fungous infections.

The parasitic diseases were represented by 299 patients (14.95 per cent), the majority of whom had scabies, so common in some parts of Italy. Our figure does not, however, show the actual incidence of parasitic infestations of overseas troops because of the fact that persons with uncomplicated infestations are treated routinely by the battalion medical officer without ever coming to the attention of the hospital dermatologists. For the same reason we have seen only a few persons with pediculosis pubis, pediculosis corporis and pediculosis capitis. Most tick bite lesions seen were fibrous nodes of long duration contracted in most cases during maneuvers in the Zone of the Interior, the chronicity being due to manual irritation.

Patients with dermatoses due to bacterial infections were found to number 236 (11.8 per cent), the fourth largest group in our series. While most reports from Africa indicate a great incidence of ecthymatous, chronic pyoderma: often called "desert sores," our impression was that in Italy the majority of pyodermic lesions

2 Pillsbury, D. M., Sulzberger, M. B., and Livingood, C. S. *Manual of Dermatology*, Philadelphia, W. B. Saunders Company, 1942, p. x.

3 Ambler, J. V. *Experience of a Dermatologist in the Southern Pacific*, *Arch. Dermat. & Syph.* 49:224 (March) 1944.

were of the most superficial variety. A large number of these impetigo contagiosa infections could be traced back to native barbers. The extreme chronicity and discouraging resistance to treatment of many cases of impetigo and ecthyma were found to be due to the patient's persistent scratching. In the background of these pyodermas, one could discover as the primary factor exposure to insect bites, a low grade contact dermatitis, psychogenic pruritus or masked scabies and sometimes lack of cooperation and conscious malingering on the part of the patient.

Patients with infectious eczematoid dermatitis were also included in this group. We have not seen any definite tuberculous disease of the skin. One patient with lupus erythematosus and 1 with lichen nitidus came under my observation.

The fifth group, with 214 patients (10.7 per cent), was composed of persons with the eczematous eruptions not directly due to infection or allergy, such as the nummular eczemas, seborrheic dermatitis, neurodermatitis (both the disseminate and the lichen simplex chronicus varieties) and also all with secondary dermatitis.

The sixth, or mixed, group, with 130 patients (6.5 per cent), was comprised of persons with various and less common cutaneous diseases. In this group we included those with malformations, purpuras, metabolic dermatoses, anomalies of pigmentation and such entities as ichthyosis congenita, vitiligo, cutis verticis gyrata, neurofibromatosis (Recklinghausen), angiokeratoma (Mibelli), porokeratosis (Mibelli) and keratosis blennorrhagica.

In the seventh group, the group with acne, there were 126 persons (6.25 per cent), including those with all types of acne. They represent only the persons with the severe types of acne coming under our observation and do not include those in whom acne was incidentally found during treatment for other diseases. While in civilian life or under fair living conditions, acne may not be a handicap in a person's occupation it may incapacitate a soldier in combat to the extent that he has to be evacuated to a hospital for treatment. The majority of this number were treated at the outpatient clinic. All patients admitted to the hospital had severe and extensive acne, requiring elaborate care. In 2 instances the disease was so incapacitating that the patients had to be transferred to a general hospital for eventual evacuation to the Zone of the Interior.

The eighth group included all the patients with common papulosquamous dermatoses, numbering 72 (3.6 per cent). The majority of this group was made up of those with psoriasis of

all types and severity, an occasional one with pityriasis rosea, patients with all types of lichen and patients with diseases of the parapsoriasis group, with diagnoses of pityriasis lichenoides chronica and pityriasis lichenoides et varioliformis acuta.

The ninth group, with 65 patients (3.25 per cent), included those with neoplastic lesions, benign and malignant. The bulk of this group consisted of persons with warts and nevi of all types. I have noted 2 patients with malignant growths in the 2,000 whose cases were analyzed. One of them was a soldier 28 years old, with a history of a previous operation for a new growth on the left side of his face and a present ulcerating squamous cell epithelioma lateral to the right eye. The other was a 32 year old soldier with a slowly developing node on the left side of his nose which was proved to be a basal cell epithelioma by histopathologic examination.

In the tenth, or virus, group, we had 28 patients (1.4 per cent). The majority of them had herpes zoster and herpes simplex. Two patients with molluscum contagiosum came under our observation.

The eleventh and last group included the patients with vesiculobullous eruptions, a total of 12 (0.6 per cent). Of this number, 6 had extensive vesiculopustular lesions of undetermined origin, 5 had dermatitis herpetiformis and 1 had pemphigus vulgaris.

The 2,000 patients whose cases were analyzed and grouped into eleven diagnostic groups were made up of persons with eighty-four separate entities, considerably less than the one hundred and eighty-nine entities in Woolhandler's report on 3,000 cases. The discrepancies in these figures may be due to the larger number of cases analyzed by Woolhandler and probably to our adherence to the more general list of army diagnostic terms.

#### TREATMENT

Soldiers whose conditions allowed treatment while on duty were treated at the outpatient clinic. However, confinement to quarters was impossible for most of the patients owing to the poor facilities offered by camps, bivouacs and other temporary quarters. Thus, all patients requiring even the shortest periods of confinement to bed or extensive medication had to be hospitalized.

In the supply of drugs and bases there was very little variety, but the few items available through our pharmacy proved to be quite adequate in the treatment of all diseases with which I had to deal.

For wet dressings we employed potassium permanganate, boric acid, resorcinol, magnesium sulfate, silver nitrate and saline solutions. Bases obtainable were petrolatum, hydrous wool fat, zinc oxide paste, boric acid ointment, zinc oxide, talc, collodion and their combinations. Incorporated in these bases the following medicinal agents were used: precipitated sulfur, resorcinol, salicylic acid, crude coal tar and ammoniated mercury. For internal and parenteral medication, sulfadiazine, penicillin, calcium gluconate, oxophenarsine hydrochloride, bismuth and autogenous blood were used.

Bacterial infections reacted well to simple compresses of solution of boric acid, bactericidal pastes and a solution of gentian violet medicinal in combination with sulfadiazine taken internally.

We could not see any definite advantage of penicillin therapy for infectious dermatoses, although we have not had extensive experience with this drug as yet. Our impression was that the chronicity of impetigo and ecthyma may have been due not so much to the failure of topical medication and of sulfadiazine, as to inadequate bandaging, insufficient instructions and poor cooperation of the patient. Mercury ointments failed often, but if the same agent was applied in a thick absorbent paste the results were more satisfactory. When medicine such as sulfonamide drugs and penicillin failed, proper hygiene of the nails and rigorous bandaging, that is, prevention of reinoculation, helped to clear obstinate infections.

Patients with scabies were treated with two to three applications of benzyl benzoate in equal parts of medicinal soft soap and alcohol. After a shower and scrubbing, the scabicide was applied from the neck down, covering every inch of the body. Its advantage over the old sulfur therapy lies in the fact that, not containing any grease, it is not messy and is more comfortable to apply, especially for ambulatory patients. Regardless of what scabicide is applied, the results depend not so much on the agent used as on the method of application and on proper instructions given to the patients. Instructions as to changing underwear or clothes are not enough to prevent reinoculation. Jewelry worn, such as rings, wrist watches and identification tags, and also the insides of shoes were cleaned with alcohol after the last application of the scabicide. All clothes worn by the patient within two weeks prior to the onset of symptoms were disinfected or laundered. A large number of patients with scabies of many months' duration, who had persistently neglected these measures, came to our attention. In many instances, the lotion or ointment was

applied only to the area of lesions and often for long periods, causing thereby a secondary dermatitis and further aggravating the condition which already had assumed a predominantly pyodermic picture.

In all cases of pruritic, infectious, parasitic and fungous diseases, the patient's finger nails and toe nails were clipped short and cleanliness of his hands was stressed. In cases of fungous infections, especially those of the hands and feet, débridement was carefully carried out. Loose particles of skin, scales, crusts and tops of vesicles were removed, and corneous thickenings, after preliminary preparation, were carefully pared off. In cases of acute trichophytosis, hot soaks, compresses and painting with 2 per cent aqueous solution of gentian violet medicinal gave satisfactory results, while ointments and keratolytics were applied only in the chronic stages of the disease. Satisfactory response to treatment in our experience depended not so much on the particular drugs applied as on the quality of nursing and general care.

We have seen some patients with "id" exacerbations, which in several instances could be traced back to indiscriminate application of salicylic acid ointments to ringworm infections. One of this group had a severe erythroderma, and another had a reaction resulting in severe exfoliative dermatitis. Both patients responded favorably after administration of 250 cc of plasma intravenously.

Psoriasis was managed by the Goeckerman therapy (combined use of coal tar ointment and ultraviolet radiation). As chrysarobin was not available, we had to rely largely on salicylic acid ointment and the rather messy coal tar ointment in the treatment of ambulatory patients. We had not seen any definite advantage in auto-hemotherapy or arsenic combined with these treatments.

Lichen planus responded readily to injections of bismuth preparations in combination with topical keratolytics, but recurrences were noted.

We refrained from the use of sulfonamide ointments, creams and powders. Thus we avoided the combined internal and topical application of these drugs which, as often reported in the literature, has frequently resulted in untoward reactions. The 2 instances of generalized dermatitis which were encountered that could be traced to simultaneous administration of sulfonamide drugs internally and topically strengthened our preference for other topical remedies.

Often the success or failure in the treatment of infectious dermatoses is believed to be due to

the use of some particular bacteriostat or bactericide. Medicines are therefore changed frequently, and recourse is taken to stronger and stronger concentrations. Our impression has been, however, that speedier cures occur not so much as a result of the kind of medicinal agent applied but as a result of its proper application plus adequate nursing and emphasis on the prevention of reinoculation. Instructions as to hygiene and proper management of lesions were given in each case, and patients were questioned persistently as to the way they followed these instructions.

Early hospitalization of outpatients who could not carry out satisfactorily the essential and sometimes comparatively simple treatments owing to their living conditions prevented eventual aggravation of their ailments and led to a more

rapid recovery, thereby saving valuable duty hours.

#### SUMMARY

Two thousand dermatologic patients were treated in a station hospital in Italy within a period of one year and their cases were analyzed. They were subdivided into eleven groups, and our statistical data for the groups were compared with those of other authors.

Problems of treatment under military conditions are discussed as well as the effect of military life on the relative incidents of cutaneous diseases.

It is felt that a report of this nature may prove of interest to medical officers in this and other theaters of operations and to civilian dermatologists.

# FIXED BULLOUS ERUPTION DUE TO SULFATHIAZOLE

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A case of fixed bullous eruption following sulfathiazole therapy is reported, with results of some allergic studies. Only one reference<sup>1</sup> can be found to a case of a similar nature, and at present this article is unavailable to us.

## REPORT OF A CASE

G S, a Negro aged 33, appeared at the dermatologic outpatient department of the University Hospital on June 16, 1943, with ten to fifteen bullous lesions of two weeks' duration on the mouth, penis, trunk and extremities. These bullae varied from 1 to 4 cm in diameter and were filled with a clear fluid. He stated

its administration the present eruption appeared. These lesions occupied precisely the sites where the bullae of the initial eruption had occurred. These facts were confirmed by communication with the patient's family physician.

*Allergic Studies*—After the eruption had subsided, passive transfer tests of the Prausnitz-Kustner type were made. In addition, blisters were raised with cantharides on normal skin and on the sites of the previous lesions. Fluid from these was used for passive transfer tests in accordance with the technic described in a previous article.<sup>2</sup> The test material included blood and blister fluid, of which 0.1 cc was injected into a nonsensitive person. Twenty-four hours later, a sulfathiazole solution was injected or a patch test with 5 per cent sulfathiazole in an oil in water



Fig 1—Fixed eruption due to sulfathiazole, lesions on glans penis

that seventeen years previously he had suffered from an attack of gonorrhea. Four years before this admission he experienced another attack of the same disease, which was treated by his own physician with sulfanilamide over a period of four months. Three months prior to this admission, because of a gonococcal reinfection, the patient was given sulfathiazole by his physician, after which a bullous eruption developed. Shortly before his admission to this clinic, sulfathiazole was administered once more, and during the time of

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1 Langhans, J. Fixed Eruption Following Therapy, *Dermat Wechnschr* 115 809-810 (Sept 26) 1942

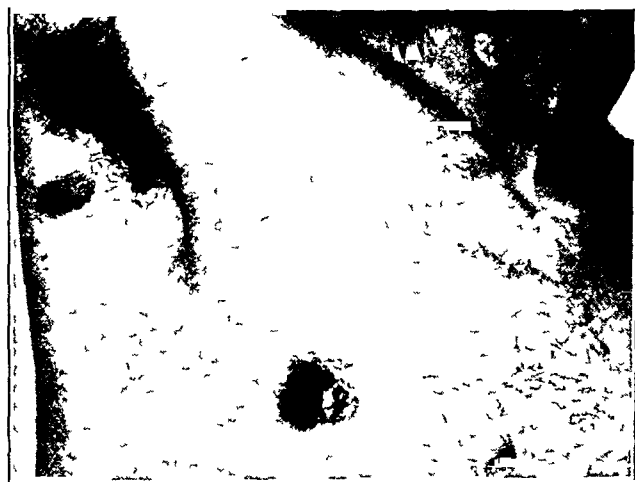


Fig 2—Fixed eruption due to sulfathiazole, sites of bullous lesions on glabrous skin

emulsion base was applied. Sites of injections were read in one-half hour and forty-eight hours. The sites of patch tests were read in forty-eight hours. Appropriate controls were employed, and these included the injections of blood and blister fluids alone, blood and blister fluids plus isotonic solution of sodium chloride, the latter alone, sulfathiazole alone and 5 per cent sulfathiazole on a patch. All reactions were negative except to the test in which blister fluid was obtained from the sites of previous lesions (sites of fixed eruption) and into which a sulfathiazole solution was subsequently injected. Both immediate and delayed reactions at those sites were positive. It was noted that at the thirty

2 Shaffer, B, Lentz, J W, and McGuire, J A. Sulfathiazole Eruptions. Sensitivity Induced by Local Therapy and Elicited by Oral Medication, *J A M A* 123 17-23 (Sept 4) 1943

minute reading the control sites where sulfathiazole was injected showed some reactions. The reactions were, however, much smaller than one which appeared at an experimental site. The reactions at two control sites were no longer present when reexamined forty-eight hours later, while a definite positive reaction was read at an "experimental" site (an indurated papule 11 mm in diameter).

#### COMMENT

While fixed eruptions to sulfanilamide have been reported,<sup>3</sup> to our knowledge this is the first report of a fixed bullous eruption due to sulfathiazole which we could substantiate. In a previous report,<sup>2</sup> we were able to demonstrate passive transfer of sensitivity by both blood and

blister fluid in cases of generalized bullous and eczematous dermatitis due to sulfathiazole.

In this case, we have shown apparently by passive transfer with blister fluid that sensitivity to sulfathiazole exists in the sites of the fixed eruption but not in the normal skin. Loveman and Simon,<sup>3a</sup> using patch tests, have demonstrated in sensitivity to sulfanilamide a similar phenomenon.

#### SUMMARY

A case of fixed bullous eruption following sulfathiazole therapy for gonorrhea was observed and studied. This diagnosis was confirmed by passive transfer tests, blister fluid from the lesion sites of the fixed eruption being used. Blister fluid obtained from the normal skin in a patient with a fixed eruption of limited distribution due to sulfathiazole elicited negative reactions to passive transfer tests.

3 (a) Loveman, A. B., and Simon, F. A. Fixed Eruption and Stomatitis Due to Sulfanilamide, *Arch Dermat & Syph* **40** 29-34 (July) 1939. (b) Goodman, M. H., and Arthur, R. D. Fixed Eruptions. Report of an Unusual Condition Due to Sulfanilamide, *ibid* **43** 692-697 (April) 1941. (c) Fowlkes, R. W., Pepple, A. W., and Vaughan, E. W. Cutaneous Reactions Due to Sulfanilamide, *South M J* **35** 1015-1016 (Nov) 1942.

# TREATMENT OF DERMATOSES WITH VASODILATORS

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An adequate supply of available oxygen is essential to the normal functioning of the cells of the body. Oxygen inadequacy may be localized to a small area so that local tissue anoxia may exist without anoxemia. Hippocrates more than two thousand years ago said "So in one place the blood stops, in another it passes sluggishly, in another more quickly. The progress of the blood through the body proving irregular, all kinds of irregularities occur." Petersen<sup>1</sup> has proved the validity of these words by showing experimentally that variation in the oxygen supply to the tissues is a common event. He believes that dysfunction of the mechanism which has to do with oxygen supply is probably the fundamental cause of disease. This report deals with results obtained in a series of patients afflicted with cutaneous diseases who were subjected to treatment designed to increase the oxygen supply of the skin.

There are many causes for interference with the normal flow of blood to the tissues. Spasm of the arterioles is an important and frequent one. Epinephrine, nicotine, histamine, emotion, cold, bacteria and alkalosis are some of the causes of vasoconstriction. Moon<sup>2</sup> has demonstrated that the normal capillary endothelium allows water and crystalloids to pass into the tissue, but when the arterioles are constricted, with resulting anoxia, the capillaries dilate and become permeable to blood cells, colloids and plasma proteins. The resultant hyperemia evidenced microscopically by vascular dilatation with perivascular cellular infiltrate is found so frequently in the early stages of many dermatoses that a vascular dysfunction underlying these diseases may be surmised. Banks<sup>3</sup> believes that scleroderma, dermatomyositis, disseminated lupus erythemato-

sus, Libman-Sacks syndrome and polyarteritis nodosa are all diffuse vascular diseases.

Nedzel<sup>4</sup> demonstrated that arteriolar spasm, although only transient in character, deprives the tissue supplied by that particular blood vessel of oxygen to such an extent that alterations are seen microscopically. These consist of dilated capillaries, perivascular edema and round cell infiltration with changes ranging from simple hyperemia to necrobiosis. His photographs clearly show the effect of vascular spasm on the tissues. The capillaries become permeable to colloids. Bacteria and other particulate matter adhere to the swollen endothelium. Anoxia "patchy" in character and occurs only in areas showing vascular damage and not in tissue only a few centimeters distant. The lesions of lupus erythematosus on the face, where sunlight may be a precipitating factor, is an example of this. Sunlight not only destroys material in the skin necessary for normal function, such as riboflavin, but it may liberate histamine which in turn damages the small blood vessels and leads to permanent abnormalities in the local circulation thus favoring the localization of bacteria.

The clinical symptoms and pathologic findings in a number of cutaneous diseases present a picture of vascular spasm. This occurs most readily in persons whose vascular system is unstable, as in the leptosome type of person. Given such a person, any one of several factors, such as infection, fatigue, emotion and meteorologic alterations,<sup>5</sup> may easily lead to vasospasm and cutaneous disease. In other words, autonomically stable persons are able to preserve their functional equilibrium in spite of a sudden chilling, but let a person not so constituted be exposed to the same trauma and vasospasm will occur in "susceptible" tissues. Such tissues are the ones that have been previously damaged by excessive sunlight or infection and occur most readily in organs possessing terminal vessels, such as the eye, brain, kidney and skin. Experiments show that the oxidation-reduction potential of the skin varies greatly in different areas, as in

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1 Petersen, W. F., and Milliken, M. E. *The Patient and the Weather*, Ann Arbor, Mich., Edwards Brothers, Inc., 1934.

2 Moon, V. H. *Shock and Related Capillary Phenomena*, New York, Oxford University Press, 1938.

3 Banks, B. M. *Is There a Common Denominator in Scleroderma, Dermatomyositis, Disseminated Lupus Erythematosus, Libman-Sacks Syndrome and Polyarteritis Nodosa?* *New England J. Med.* **225**: 433 (Sept 18) 1941.

4 Nedzel, A. J. *Vascular Spasm*, Urbana, Ill., University of Illinois Press, 1943.

5 Schmidt, F. R. *Skin Diseases and the Weather*. *Arch. Dermat. & Syph.* **32**: 781 (Nov.) 1935.



the flexor surfaces compared with the extensor surfaces.<sup>6</sup> This difference in oxygen requirement may be relative, for it is the disparity between the need for oxygen and its available supply that is the determining factor. Wherever local anoxia or increased metabolism or both prevail localization of lesions may occur.

For a few years I<sup>7</sup> used iodine therapeutically in an attempt to overcome vasospasm and improve the circulation of the skin. Vasodilatation with improved tissue oxidation was obtained in some early cases of psoriasis, alopecia areata and summer pruritus. I wish to stress the importance of treating these diseases early in their course, for late pathologic changes in the tissues exclude the possibility of returning the cells to normal.

During the past year I have treated 55 patients with diseases of the skin with substances that

tive and economical and was therefore used in the majority of cases. It should be given with meals to avoid excessive flushing and tingling of the skin. Sodium nitrite intravenously in 100 mg doses was used in acute cases of purpura and erythema multiforme with good results.

Determinations of blood pressure were made whenever possible.

#### COMMENT

The results observed with this therapeutic modality are encouraging, provided that treatment is instituted early in the course of the disease. The rapid involution of so-called inflammatory dermatoses such as purpura, summer prurigo, erythema multiforme, erythema nodosum and toxic erythema was striking and should stimulate the employment of these drugs

TABLE 1—Summary of Data on Patients with Dermatoses Treated with Vasodilators

| Disease  | Average Duration of Disease                     | Number of Cases | Results   | Comment   |
|--|---|-----------------|---|---|
| Psoriasis  | 5 years   | 6               | Unimproved  | No early cases encountered in this series               |
| Itching of legs with peripheral vascular disease | 6 months  | 8               | Improved  |   |
| Summer prurigo                                   | 2 years   | 2               | Rapid improvement   | Lesions disappeared quickly<br>Itching stopped promptly |
| Erythema multiforme                              | 1 day to 3 weeks                                | 7               | Rapid improvement   |   |
| Toxic erythema from drugs                        | 2 days  | 3               | Rapid improvement   |   |
| Urticaria  | 3 days to 4 years                               | 8               | Improvement in early cases only                           |   |
| Pityriasis rosea                                 | 6 days after appearance of generalized eruption | 4               | Rapid involution of lesions in 1 case of 2 days' duration |   |
| Purpura  | 5 days  | 2               | Rapid improvement   | No disseminated cases were treated                      |
| Erythema nodosum                                 | 1 week  | 2               | Rapid improvement   |   |
| Alopecia areata                                  | 2 months  | 2               | Hair stopped falling out                                  |   |
| Herpes simplex                                   | 3 days  | 5               | Undetermined  |   |
| Herpes zoster                                    |   | 5               | Undetermined  |   |
| Lupus erythematosus                              | 3 years   | 4               | Undetermined  | Itching controlled                                      |
| Cold allergy                                     | 2 years   | 1               | No attacks while taking nicotinic acid                    |   |
| Dermatitis herpetiformis                         | 3 years   | 1               | Improvement   |   |

induce vasodilatation. These included nicotinic acid, nicotinamide, acetylcholine, sodium nitrite, erythrityl tetranitrate, typhoid vaccine and estrogen. Following the advice of Duggan<sup>8</sup> and Cordes,<sup>9</sup> who secured excellent results with these drugs in a number of ocular diseases, patients are forbidden to use tobacco and exposure to cold is to be avoided, as should also psychic trauma, worry and excitement. One teaspoon of cider vinegar in one-half glass of water, three times daily, is also prescribed. Nicotinic acid in doses of 50 to 100 mg three times daily proved effective

by those who may have the opportunity to study early instances of scleroderma, dermatomyositis, disseminated lupus erythematosus, acrodermatitis atrophicans and angioneurotic edema. In addition, I believe that erythrocytosis of the legs in young girls and in some cases cold allergy and pityriasis rosea might react favorably to vasodilators.

These studies suggest the possibility of securing better penetration into the skin of a substance like a gold compound as used in the treatment of lupus erythematosus. Chambers and Bernton<sup>10</sup> have recently found that patients with urticaria were more promptly relieved of symptoms if calcium gluconate was administered in conjunction with nicotinic acid.

Lately, I have found that the administration of other water-soluble vitamins such as thiamine

6 Schmidt, F R. Blood and Oxygen Supply of the Skin, Arch Dermat & Syph 32:576 (Oct) 1935

7 Schmidt, F R. The Action of Iodine on Diseases of the Skin as Influenced by Season and Weather, Arch Dermat & Syph 42:1083 (Dec) 1940

8 Duggan, W F. Clinical Vascular Physiology of the Eye, Am J Ophth 26 354 (April) 1943

9 Cordes, F C. The Use of Vasodilators in Acute Fundus Disease, Am J Ophth 26 916 (Sept) 1943

10 Chambers, D C, and Bernton, H S. The Administration of Nicotinic Acid and Calcium Lactate in Urticaria, J Allergy 15 141 (March) 1944

and riboflavin along with nicotinic acid appears to augment the beneficial effects of nicotinic acid alone. This may be explained by recalling that thiamine acts by potentiating the action of acetylcholine, the vasodilator hormone of the body. Moreover, nicotinic acid, thiamine and riboflavin apparently play an important role in the oxidation of carbohydrate in the central nervous system.

The rapid involution of certain lesions observed in this series of patients when nicotinic acid was administered finds corroboration in the work of other investigators. Bean, Spies and Vilter<sup>11</sup> reported that pellagrous dermatoses dis-

appear quickly following oral administration of nicotinic acid.

It is suggested that persons suffering from livedo reticularis with ulcerations be subjected to vasodilator treatment, in lieu of sending them to a place of high altitude and low barometric pressure.

#### SUMMARY

Results obtained with vasodilators in the treatment of 55 patients afflicted with diseases of the skin suggest their further employment in a large series of cases. The most favorable response to vasodilators was observed in dermatoses characterized by so-called inflammatory lesions, thus substantiating the assumption of their arteriolar-capillary origin.

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<sup>11</sup> Bean, W. B., Spies, T. D., and Vilter, R. W. Asymmetrical Cutaneous Lesions in Pellagra, *Arch Dermat & Syph* **49** 335 (May) 1944.

# PIGMENTATION OF HAIR ON TRANSPLANTED SKIN IN HOODED RATS

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While making some studies on the pigmentation of hair in piebald rats and exchanging areas of skin producing black hair with areas having white hair, my colleagues and I noted that the skin which formerly grew black hair often produced white hair in its new environment. In other rats areas of skin producing black hair were then incised and sutured back in their original sites, and they often produced white hair. The latter experiments showed that the white hair on the transplants was due to changes resulting from the operation rather than to the environment.

These results differed from the observations made on guinea pigs by Seevers and Spencer,<sup>1</sup> who found in 52 successful grafts that transplantation of skin from a colored area to a white area showed that the hair follicles do not lose their pigment-producing potentialities in an unpigmented area. Lewin and Peck,<sup>2</sup> in similar experiments on guinea pigs, found that dark skin transplanted to a white skin area usually produced no hair. Any hair that was present on the graft or was regenerated retained the characteristics and color of the original site. However, in some instances, white hair of poor quality developed in the center or was scattered through the graft.

The skin of hooded rats differs from the skin of guinea pigs. Unpigmented skin produces black hair in rats, while black hair grows in pigmented skin in guinea pigs. The skin of a hooded rat is, therefore, quite comparable to the skin covering the head of a white man.

To determine whether or not the white hair on the transplanted skin and the incised skin was due to a disturbance of the vascular or of the nervous relations, areas of skin producing black

hair were denervated in some animals. All observations indicated that the white hair resulted from depriving the skin of its vascularity.

By following the growth of the hair for several cycles<sup>3</sup> on the transplanted and the incised areas, it was evident that the cells of the hair bulbs were unable to regain their ability to form pigment once they had lost it.

The descriptions of the grafts and the conditions which have induced the white hair and which may be responsible in many instances for the graying of hair in mammals with age are of such interest that they seem to warrant reporting.

## EXPERIMENTAL PROCEDURE

Piebald rats of the Long-Evans strain were used in these experiments. When the animals were 22 days old, the hair was removed from a region producing black hair and a region producing white hair with sodium sulfide.

With the animals under ether anesthesia areas of skin, approximately 0.75 cm square and thick enough to include the panniculus carnosus, were incised and then interchanged between the regions. The grafts were held in place with interrupted sutures and coated with petrolatum to prevent drying, as in previous transplantation experiments.<sup>4</sup> Twenty-five such interchanges were made, and in 19 instances both transplants survived. The grafts usually persisted if they had a white pinkish color seventy-two hours after the interchange.

When the next growth of hair appeared externally on the grafts, usually about the age of 38 days,<sup>5</sup> many gradations in pigmentation and in quality of the hair existed on the areas which formerly produced black hair. These grafts will now be described.

Figure 1 shows a transplant covered almost entirely with fine white hairs except for the few black hairs around the periphery of the graft. The area of this graft has enlarged slightly since the time of transplantation.

From the Departments of Anatomy, College of Dentistry and the Graduate School of Arts and Science, New York University.

1 Seevers, C. H., and Spencer, D. A. Autoplastic Transplantation of Guinea Pig Skin Between Regions with Different Characters, *Am. Naturalist* **66** 183-189, 1932.

2 Lewin, M. L., and Peck, S. M. Pigment Studies in Skin Grafts on Experimental Animals, *J. Invest. Dermat.* **4** 482-505, 1941.

3 Butcher, E. O. The Hair Cycles in the Albino Rat, *Anat. Rec.* **61** 5-19, 1934.

4 Butcher, E. O. Hair Growth on Skin Transplants in the Immature Albino Rat, *Anat. Rec.* **64** 161-171, 1936, Fate and Activity of Autografts and Homografts of Skin in White Rats, *Arch. Dermat. & Syph.* **36** 53-56 (July) 1937.

5 Butcher, E. O. Hair Growth in Adrenalectomized, and Adrenalectomized Thyroxin-Treated Rats, *Am. J. Physiol.* **120** 427-434, 1937.

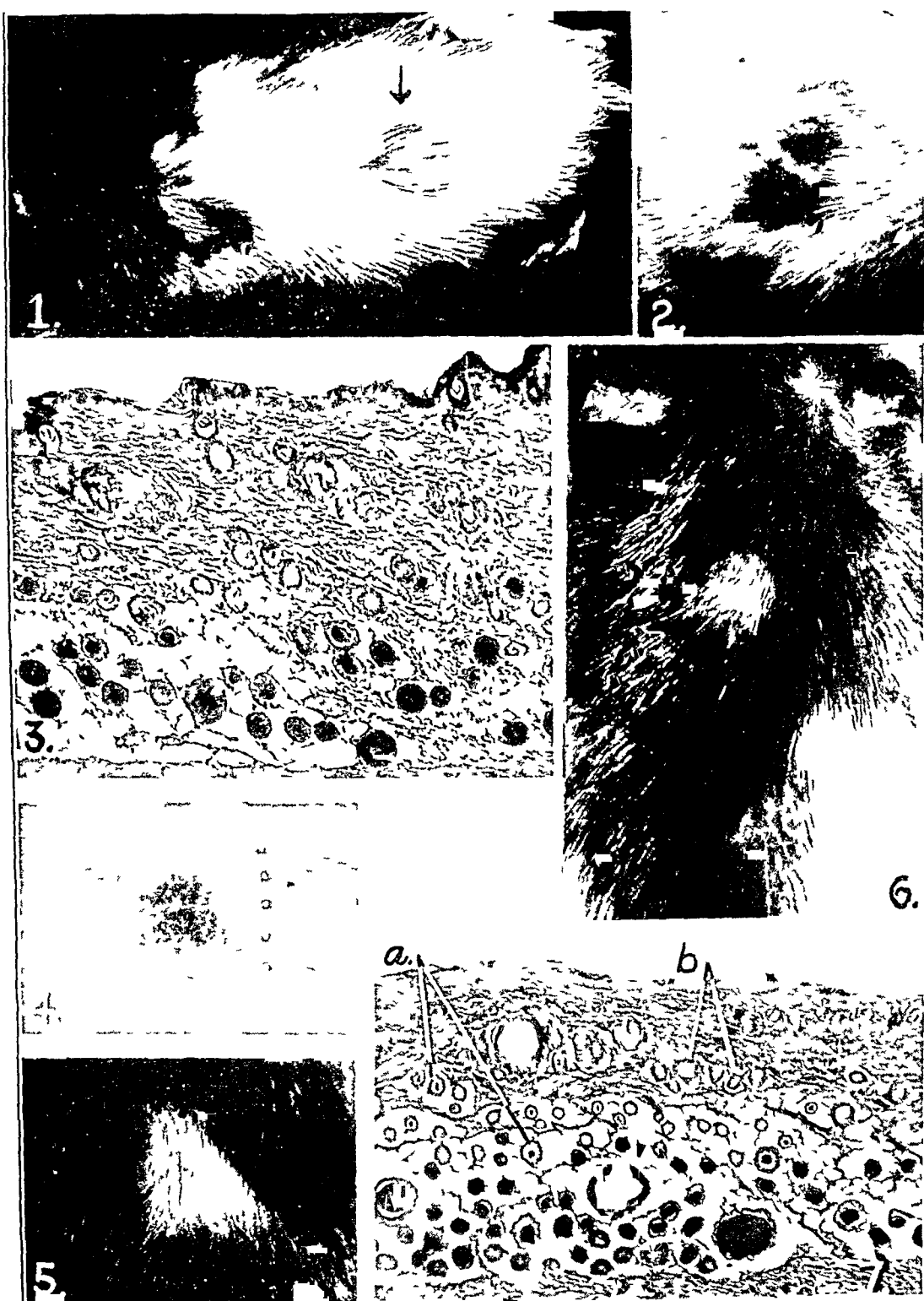


Fig 1—An area which formerly produced black hair now has fine white hairs

Fig 2—This graft has a band of white hair

Fig 3—A histologic section of the graft shown in figure 2 On the right side of the photograph dense and cellular tissue is associated with white hairs  $\times 80$

Fig 4—The anterior part of this graft is producing black hair while the posterior part has white hair The dotted line marks the posterior limit of the graft

Fig 5—An area was incised and sutured back in this hooded rat, and it produced white hair

Fig 6—This photograph shows an area which was incised and sutured in the original site

Fig 7—A histologic section of the left side of the graft shown in figure 5 Black hairs (a) are on the left and white hairs (b) on the right side  $\times 70$

In figure 2 is seen a graft which enlarged from the time of transplantation and which has a band of white hair running through it. All the hairs on this graft are coarse and good in quality. The hair has been cut away around the graft to show the extent and condition of the transplant. Figure 3 shows a histologic section through the graft. Associated with the white hairs on the right side of the photograph is a dense and cellular subcutaneous tissue which has replaced the loose fatty tissue. It seems possible that this dense tissue may in some way be responsible for the failure of follicles in this region to produce pigment. While dense tissue is sometimes found associated with the lack of pigmentation, cases are equally common in which there are no changes in the subcutaneous tissue and yet a lack of pigmentation exists.

Figure 4 shows a graft which has enlarged considerably since the time of interchange. The anterior part of this graft is producing black hair while the posterior part, the posterior limit of which is indicated with a dotted line, has white hair. The quality of the hair on the two parts is similar. The animal bearing the graft shown in figure 4 was killed, and its vascular system was injected with india ink. The transplant and the surrounding skin were then fixed in Bouin's fluid, cleared and spread on a slide. Tracings of the vascular channels were made with a projector, and no differences in the vascular supply of the two parts could be found. Histologic sections of the two parts also were very similar, and no differences in the distribution of collagenous and elastic fibers, in the amount of adipose tissue or in the structure of blood vessels could be found which would account for the lack of pigmentation. Histologic sections of grafts from other rats confirmed these observations.

In the previous experiments there existed the possibility that the region surrounding the transplanted area in some way induced the lack of pigmentation.

To test this possibility, areas of skin were completely incised in regions producing black hair and then sutured back in their original positions. Rats 22 days old with hair follicles in the resting stage were again used for these experiments. Figure 5 shows a typical result of such an operation in a hooded rat. The graft has enlarged since the operation and is producing white hair of good quality. No histologic differences exist in sections (fig. 7) taken at the junction of the incised skin with the surrounding skin. The result of a similar operation on a piebald rat is seen in figure 6. In this instance there has been a shrinkage of the incised area, which is producing white hair of good quality.

One might have thought that the cells would have recovered their pigment-forming potentialities with the establishment of the blood supply and would have again produced black hair. This was, however, not the case, for the incised areas and grafts on the piebald animals continued to produce white hair in the successive hair cycles.<sup>3</sup>

Irritants (xylene, benzoic acid and capsicum) were applied daily to some of the transplanted areas to determine whether increased vascularity and an edematous condition would induce the cells of the hair bulbs to form pigment again. No increased pigmentation resulted in the successive growth cycles. Lewin and Peck<sup>2</sup> also failed to increase the pigmentation of guinea pig skin with applications of ultraviolet rays. Pantothenic acid, the antigreying factor<sup>6</sup> in rats, was dissolved in Pentrasol A<sup>7</sup> (60 mg of calcium pantothenate to 5 cc of Pentrasol A) and applied to the grafts producing white hair during the successive cycles, and no increased pigmentation resulted.

There existed the possibility that the lack of nerve supply was responsible for the lack of pigmentation in these incised areas, since interference with the nerve supply has been associated with the depigmentation of skin in leprosy.<sup>8</sup> To test this possibility incisions were made through the skin (including the panniculus carnosus) on each side of the body from the middle of the axilla anteriorly to the thigh posteriorly. A scalpel was then inserted under the skin (beneath the panniculus carnosus), and all the branches of the spinal nerves and peripheral blood vessels were sectioned to this large region of skin over the dorsum of the rat. The incisions were sutured, and they quickly healed. Blood was then supplied to the dorsal region from anterior and posterior vascular channels, which were seen to hypertrophy quickly. No necrotic areas resulted in this large region, and the usual pattern of pigmented hair appeared with the cyclic growth over the back.

Some sympathetic nerves possibly coursed along with the blood vessels into this dorsal region, and some investigators might claim that the region was not entirely denervated. It

6 Emerson, G. A., and Evans, H. M. Growth and Graying of Rats with Total "Filtrate Factor" and with Pantothenic Acid, *Proc Soc Exper Biol & Med* **46**: 655-658, 1941.

7 Herrmann, F., Sulzberger, M. B., and Baer, R. L. New Penetrating Vehicles and Solvents, *Science* **96**: 451-452, 1942. Pentrasol A consists of 20 Gm of Aerosol MA and 20 cc of xylene warmed under reflux until a glassy gel results. This gel is taken up with 20 Gm of antipyrine and 80 cc of propylene glycol.

8 Boyd, W. A. *Textbook of Pathology*, ed. 4, Philadelphia, Lea & Febiger, 1943.

would seem, however, that such incisions would have had some effect on the pigmentation if the nerves were responsible for the lack of pigmentation in the new growth of hair. The rats had no sensation in this dorsal region which had been incised laterally. If the lack of nerves were responsible for the absence of pigmentation, it would be difficult to explain the presence of patches of black hair completely surrounded by white hair on some of the transplanted areas. In these cases the nerves in all probability would grow in from the periphery and the pigment-forming cells would be more apt to survive in the periphery than in the center of the graft.

Thus there was no evidence that the lack of nerves was associated with the lack of pigmentation.

The areas on which white hair normally grew and which were transplanted into regions producing black hair continued to produce white hair of a variable quality.

#### SUMMARY

When skin producing black hair is interchanged with skin producing white hair in the piebald rat, white hair frequently grows on the skin which formerly had black hair. Likewise, if skin producing black hair is incised and sutured back in place, it often produces white hair.

The present conception of pigment formation seems to be that pigment results from the combination of a chemical substance, or propigment, carried by the blood with an enzyme in the cells of the hair bulb. In these rats the propigment was present, since the rest of the hair of the

animal remained black and black hairs often appeared among the white ones on the grafts. The white hair was not due to the lack of innervation, as was shown by denervating areas. The enzymatic potentialities of the cells of the hair bud must, therefore, have been affected by the lack of vascularity and nutrition immediately following the operation, since injection studies show that the vascular supply of the graft soon becomes similar to the supply of the surrounding skin.

Once the pigment-forming ability is lost by the cells, there is no restitutive capacity. Application of irritants to the skin has failed to induce the cells of the hair buds to form pigment again.

Growth or production of the hair by the hair bud is also affected by vascularization. Increased blood supply accelerates hair growth.<sup>9</sup> Growth is not affected permanently by poor blood supply, as shown in these experiments, while the pigment-forming capacities of the cells are affected permanently.

When the skin was incised, all blood supply was eliminated. Nutrition was supplied to the graft by tissue fluid from below the graft and from around its periphery. This tissue fluid sufficed to supply the cells of the hair bulb with nutrition necessary for the survival of their growth potentialities. The tissue fluid, however, did not provide the cells with the substances necessary for the survival of their enzymatic potentialities. Thus, the requirements for growth are less than for pigment formation.

9 Butcher, E. O. The Effects of Irritants and Thyroxin on Hair Growth in Albino Rats, *Am J Physiol* **129** 553-559, 1940.

# LICHEN SCLEROSUS ET ATROPHICUS IN CHILDHOOD

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Lichen sclerosus et atrophicus is ordinarily a disease of adults. It occurs most frequently in middle-aged women, although no relationship to the menopause has ever been established. The observation of 3 cases of lichen sclerosus et atrophicus in young girls within a short period is noteworthy and constitutes the basis of this report.

## CLINICAL FEATURES

Within the past fifteen years there have been two detailed discussions in the American literature concerning lichen sclerosus et atrophicus and related disorders such as guttate morphea and atrophic lichen planus, that of Nomland<sup>1</sup> in 1930 and that of Montgomery and Hill<sup>2</sup> in 1940. These observers have done a good deal to clarify the utter confusion which previously existed in connection with these diseases, especially as to terminology. Montgomery and Hill were correct in urging the abandonment of the terms "white spot disease" and "caid-like scleroderma of Unna" which were used loosely to include both morphea and lichen sclerosus atrophicus. Lichen albus of Zumbusch and chronic atrophic lichenoid dermatitis of Csillag are terms which have also been used to describe lichen sclerosus et atrophicus. It is the consensus now that the disease is not a form of atrophic lichen planus, so that the terms lichen planus sclerosus or lichen planus sclerosus et atrophicus are obsolete and no longer acceptable in modern nomenclature.

The primary lesion in lichen sclerosus et atrophicus is an achromatic, irregular or polygonal flat papule. In well developed cases the

individual papules coalesce to form ivory-colored plaques of various sizes and shapes, although in many cases both the plaques and the individual papules may be seen. The lesions may be on the same plane as the neighboring normal skin or slightly elevated. Most typical lesions present tiny comedolike plugs studding their shining and otherwise smooth surfaces, although such follicular plugs are not absolutely essential to the clinical diagnosis. Even when they are not obvious grossly, however, they may be seen in microscopic sections. Delling of the lesions may be present, and in old patches of



Fig 1—Lichen sclerosus et atrophicus with involvement of the vulva and perianal region in a girl aged 4½ years

the disease the skin may be atrophic, resembling parchment.

The favorite sites of involvement are the upper parts of the trunk, especially the sternal and clavicular areas, the neck, axillas, forearms and anogenital region. The disease is commonly limited to the vulva and perianal areas. It is the opinion of Freeman and me<sup>3</sup> that lichen

From the Division of Dermatology, University of Minnesota, H E Michelson, M D, Director

1 Nomland, R. Lichen Sclerosus et Atrophicus (Hallopeau) and Related Cutaneous Atrophies, Arch Dermat. & Syph 21 575 (April) 1930

2 Montgomery, H, and Hill, W. Lichen Sclerosus et Atrophicus, Arch Dermat & Syph 42 755 (Nov) 1940

3 Freeman, C, and Laymon, C W. Balanitis Xerotica Obliterans, Arch Dermat & Syph 44 547

(Footnote continued on next page)



sclerosus et atrophicus can likewise occur on the male genitals as isolated papules on the shaft and/or sclerotic preputial and urethral involvement. Both types of genital involvement may occur alone or with lesions elsewhere on the body. Cases of this type have usually been reported under the title *balanitis xerotica obliterans*.

The disease is a rarity in the young. In Montgomery and Hill's large series of 46 cases,



Fig 2—Histopathologic features of lichen sclerosus et atrophicus: hyperkeratosis, epidermal atrophy, zone of homogenization in the papillary portion of the cutis and zone of lymphocytic infiltration beneath.

only 1 began in a girl aged 10. There were 3 cases in patients in the late twenties, 4 in persons in the thirties and all of the rest occurred in patients in the fourth to the seventh decades of life. Many dermatologists were questioned, but none could remember seeing a case in early childhood.

Regardless of age of onset the course of the disease is long and treatment is of no avail. The cause is unknown.

(Oct.) 1941 Laymon, C W, and Freeman, C. Relationship of Balanitis Xerotica Obliterans to Lichen Sclerosus et Atrophicus, *ibid* 49:57 (Jan.) 1944.

#### HISTOPATHOLOGIC FEATURES

Well developed lesions of lichen sclerosus et atrophicus have histopathologic features which are pathognomonic. Perhaps the most striking is the band of homogenization directly beneath the epidermis. Montgomery and Hill regarded this as lymphedema rather than true sclerosis in the sense that there is a true increase in connective tissue. The elastic fibers are split but not destroyed. Beneath the homogenized area in most cases is a bandlike zone of lymphocytic infiltration. This feature is not present in all cases, and in early lesions the infiltrate may be situated only about dilated blood vessels. Obliterative changes of the deep vessels, as seen in scleroderma, are not present in lichen sclerosus et atrophicus.

The epidermal changes consist of hyperkeratosis, keratotic plugging of the follicles and atrophy of the rest of the epidermis with flattening of the rete pegs. There may be vacuolization and mild liquefaction degeneration of the basal layer.

#### REPORT OF CASES

CASE 1—B P, a white girl aged 6 years, was first seen in February 1943. Her mother had noted lesions on the child's vulva about fifteen months previously, shortly before her fifth birthday.

On examination there were achromatic, sclerotic plaques surrounding the vulva and extending posteriorly over the perineum to the anus but not encircling it. The labia minora appeared shrunken. There were several fissures on the surface of the lesions on the perineum. There were no other abnormalities on the rest of the skin or mucous membranes.

A biopsy was performed, and the histopathologic changes confirmed the clinical diagnosis of lichen sclerosus et atrophicus.

The child was reexamined at approximately monthly intervals until October 1944. After a trial of arsenic therapy (asiatic pills) and vitamin A orally with bland lubricating ointments topically there was moderate improvement. At the time of the last examinations the affected skin was somewhat more pliable, and there have been no fissures for several months.

CASE 2—S D, a white girl aged 4½ years, was first seen in December 1944. Lesions about the vulva had been present for one month. For the same period the child had complained of difficulty and discomfort at the time of defecation.

On examination the vulva and perianal region appeared to be surrounded by a zone of depigmentation. On palpation, however, it was obvious that the ivory-colored areas were inflexible and somewhat sclerotic. There were no other lesions on the body.

The histopathologic changes confirmed the clinical diagnosis of lichen sclerosus et atrophicus.

The child was given vitamin A orally and a lubricating ointment, and when she was again examined three and one-half months later the appearance seemed unchanged although there was no discomfort at the time of defecation

CASE 3—S W, a white girl who had just passed her fourth birthday, was seen in June 1945. Yellowish white areas were first noted in the perianal region three months previously.

Examination showed lesions on the vulva, perineum and perianal region practically identical with those in the previous 2 cases. There were several fissures and erosions about the anus. Numerous telangiectatic blood

vessels coursed over the slightly shriveled labia minora. The rest of the skin was normal.

The histopathologic changes were consistent with the clinical diagnosis of lichen sclerosis et atrophicus.

The patient has not reported for subsequent examination.

#### SUMMARY

Lichen sclerosis et atrophicus, although predominantly a disease of middle-aged women, can occur in young children. In 3 cases in girls below the age of 6 years the lesions were limited to the anogenital region.

# DIFFERENTIATION OF LEPROMATOUS FROM "NEURAL" LEPROSY

## THE BASIS, A METHOD, AND REPORT OF FIVE CASES

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The diagnosis of leprosy should in most cases permit a prognosis to be made as well. This offers three important advantages to the physician. It enables him to decide on the disposition of the case, whether to isolate or merely observe, it permits him to evaluate the effect (if any) of treatment, and it permits him (if it is favorable) to soften the blow when he informs the patient of the diagnosis.

These advantages can be accomplished only by making an exact diagnosis—that is, not merely "leprosy," but "leprosy, lepromatous," or "leprosy, 'neural'." Lepromatous leprosy has a bad prognosis for arrest or recovery, "neural" leprosy has a good prognosis for arrest or recovery. It is rare for the disease to undergo transition from either type to the other, and it is probably impossible for a patient to present both types simultaneously. The term "mixed leprosy" was never intended to mean *mixed types* of the disease, it really means lepromatous leprosy in *mixed sites of involvement* both skin and nerves. Inasmuch as virtually every patient with leprosy of whatever type presents lesions of both the skin and the nerves, the term is an unnecessary and confusing one, and should be abandoned.

This basic distinction between the two types of leprosy can usually be made without difficulty, even in comparatively early cases, and it is with this differentiation that this paper will be primarily concerned.

### LEPROMATOUS LEPROSY

Lepromatous leprosy is the form of the disease once known as elephantiasis, leontiasis, or satyriasis, Graecorum. Avicenna is said<sup>1</sup> to have suggested that the first two of these names stemmed from the fearful and terrifying appearance of the faces in advanced cases. Aretaeus, too, said the name elephantiasis was applied to leprosy because it was "disgusting to the sight,

and in all respects terrible, like the beast of similar name." More recent synonyms for this form of leprosy are "tubercular leprosy" (i.e., leprosy characterized by tubercles or nodules) and "cutaneous leprosy", the latter term was the official one from 1931 to 1938, being adopted because of the tendency of this form of the disease to involve the skin somewhat more conspicuously, in most cases, than the nerves.

Lepromatous leprosy is characterized primarily by red, elevated, granulomatous infiltrations of the skin which are called lepromas (fig 1). More diffuse infiltrations may also



Fig 1—Typical "lepromas" of helix and antitragus of ear. Below the ear is seen a swelling caused by acute lepromatous neuritis of the right great auricular nerve.

occur. These lesions are typically rich in *Mycobacteria leprae*, and are never free from them except perhaps in the transitory earliest stages or in advanced retrogression. These granulomas occur in the skin, in nerves and in virtually all of the reticuloendothelial structures of the body—lymph nodes, testes, bone marrow, liver and spleen. Mitsuda<sup>2</sup> has observed lepromatous infiltration also in the heart, stomach, intestine,

Read at the Annual Meeting of the California State Medical Association, Los Angeles, May 6, 1945.

1 Avicenna, in Bateman, T. A Practical Synopsis of Cutaneous Disease, ed 1, Philadelphia, Collins & Croft, 1818.

2 Mitsuda, K., and Ogawa, M. A Study of One Hundred and Fifty Autopsies on Cases of Leprosy, Internat J Leprosy 5:53 (Jan-March) 1937.

kidney, urinary bladder, ovary and other sites. The conjunctiva, cornea, nasal mucous membrane, pharynx and larynx are also frequently involved in advanced cases. The cutaneous lesions of early lepromatous leprosy resemble urticaria more regularly and more closely than they do any other one disease, they rarely manifest hypopigmentation or annular configuration, and when advanced they frequently mimic with remarkable fidelity the clinical appearance of lymphoblastoma of the skin, either the nodular or the diffusely infiltrative type.

Neurologic changes are present in virtually every case of lepromatous leprosy. As in "neural" leprosy, these may vary from anhidrosis, thermal anesthesia, dermatographism or alopecia (chiefly of eyebrows), through total anesthesia and muscular weakness, to muscular paralysis and atrophy and contracture, trophic absorption of bone and trophic ulceration. Cutaneous nerve damage in lepromatous leprosy, unlike that in "neural" leprosy, has no particular tendency to occur in the skin overlying the leprous cutaneous lesions, or to coincide in extent with such lesions, this occurrence is infrequent enough to be attributed to coincidence.

The other clinical manifestations of lepromatous leprosy—ocular and laryngeal involvement—are seen only in advanced cases, they eventuate in, respectively, blindness and laryngeal stenosis, the latter requiring tracheotomy.<sup>3</sup> Enlargement of the lymph nodes seldom attracts attention, and the other visceral lesions rarely if ever reach the clinical threshold. A notable exception to this is amyloid disease, which is regularly found at autopsy in the kidneys, liver and spleen, and apparently explains a large proportion of the deaths from "chronic nephritis," which is the assigned cause of death in about one sixth of most series of cases. In Hawaii, at least, it is felt that this is not the result of the frequently associated tuberculosis, for it is almost never seen in autopsies on nonleprous patients at the Leahi Hospital for tuberculosis in Honolulu.<sup>4</sup>

Histologically, the lesions of lepromatous leprosy consist of diffuse granulomatous infiltration composed of round and spindle-shaped histiocytes which are often loaded with fat and almost always with *Myco leprae* (fig 2). Their cytoplasm is foamy, some of them are vacuolated, and a few are multinucleated. The general appearance closely simulates that of xanthoma tuberosum. In nerves, there is typically only a

sparse inflammatory infiltrate with fairly numerous vacuolated cells, and large numbers of bacilli. The relative lack of inflammatory reaction is in striking contrast to the picture seen in the nerves in "neural" leprosy, and suggests that permanent damage to an involved nerve might be expected to occur less often in the lepromatous form of the disease than in the "neural" form. Tilden<sup>4</sup> has recently reviewed lepromatous leprosy thoroughly from the histologic standpoint.

The lepromin (Mitsuda) test is regularly negative in lepromatous leprosy. This test consists of the intradermal injection of 0.1 cc of a phenolized suspension of heat-killed *Myco leprae* in isotonic solution of sodium chloride. This is usually prepared by grinding an amputated lepromatous ear lobe in a mortar with saline solution, the resultant suspension is filtered, autoclaved and phenolized. A positive reaction to the test consists of an elevated, infiltrated, erythematous papule 1 cm or so in diameter, which frequently ulcerates at the center. The mature reaction usually requires about three weeks to develop.

Positive reactions to serologic tests of the blood for syphilis occur, according to Hopkins and Faget,<sup>5</sup> in 56.4 per cent of cases of "mixed" leprosy and in 60.2 per cent of cases of lepromatous leprosy without severe nerve damage. The close correspondence of these figures with one another is additional evidence of the futility of establishing separate categories for lepromatous cases with and without "marked" nerve damage. These authors also confirmed Badger's statement<sup>6</sup> that the proportion of positive reactions was higher among patients with active leprosy, particularly in those undergoing a lepra reaction.

Lepromatous leprosy is characterized by the occurrence at irregular intervals of the lepra reaction. This phenomenon consists of fever, neuralgia and erythema multiforme, the last usually takes the form of either severe erythema nodosum or, less frequently, erythema multiforme bullosum. Such lepromatous lesions as are already present are likely to become swollen and more erythematous, and often ulcerate. New lesions may appear. The sedimentation rate increases. The patient is acutely ill, and remains so for a variable period, usually a few weeks. He then gradually recovers from the

<sup>3</sup> Sloan, N. Tracheotomy in Leprosy, *Internat J Leprosy*, to be published.

<sup>4</sup> Tilden I. L. Lepromatous Leprosy. A Reticulo-endothelial Disease. *Am J Clin Path* 15:165 (May) 1945.

<sup>5</sup> Hopkins, R., and Faget, G. H. Recent Trends of Leprosy in the United States, *J A M A* 126:937 (Dec 9) 1944.

<sup>6</sup> Badger, L. F. Significance of Positive Wassermann and Kahn Reactions in Leprosy, *Pub Health Rep* 46:957 (April 24) 1931.

reaction, and returns to about the same condition in which he was before it occurred. Individual lesions may look somewhat improved, but his general condition is usually worse, and his

The prognosis of lepromatous leprosy is poor for recovery or even arrest. Gradual or intermittent progression of lesions is the rule, eventually laryngeal stenosis develops, and progresses

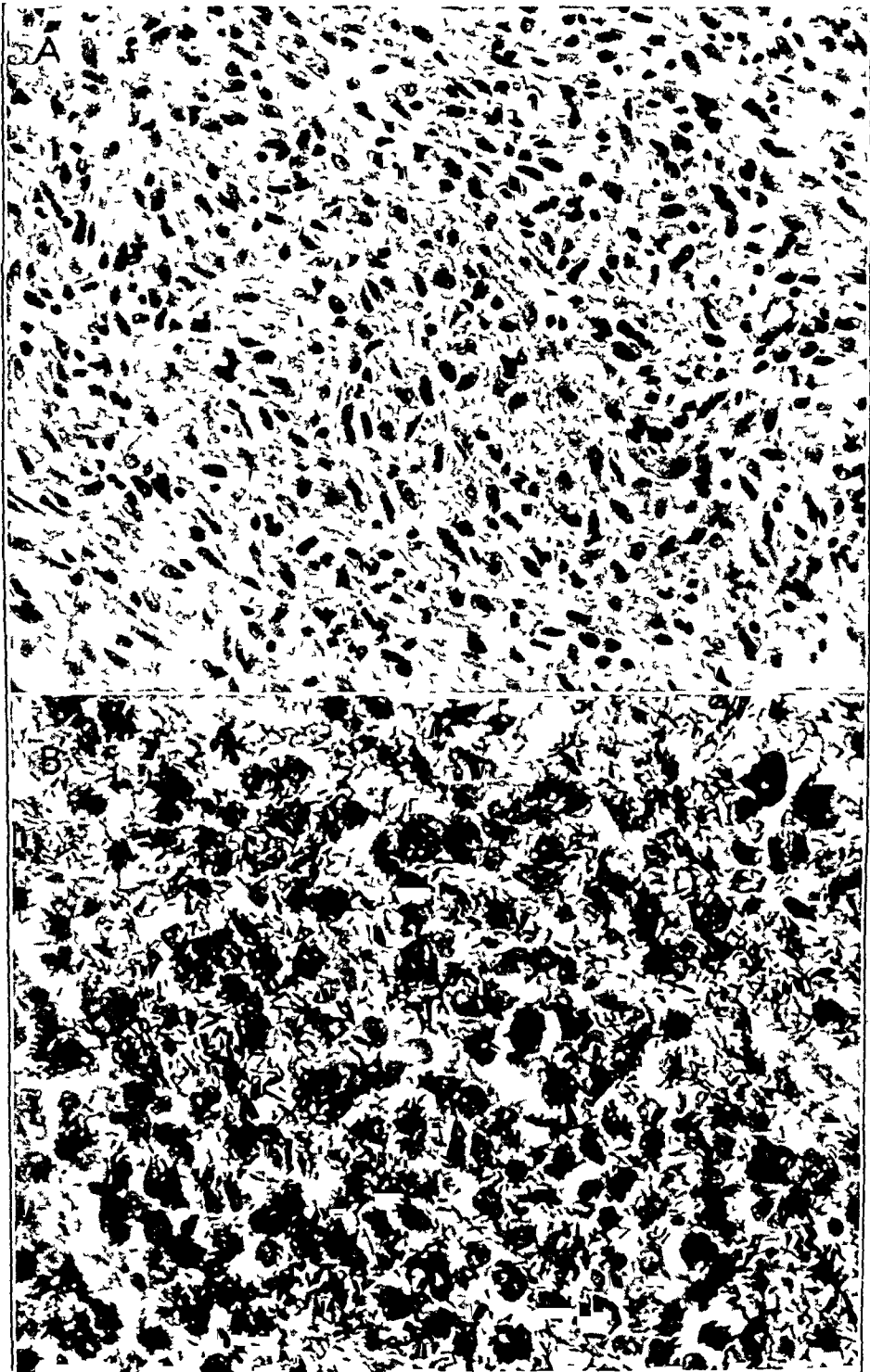


Fig 2—*A*, xanthoma-like infiltrate of lepromatous leprosy. Hematoxylin and eosin,  $\times 300$ . *B*, granulation tissue of lepromatous leprosy showing abundance of leprosy bacilli. Fite's fuchsin-formaldehyde,  $\times 600$ .

lesions more extensive, than before. Such reactions may be precipitated by the menarche, an individual menses, pregnancy or an intercurrent illness. They may also occur without any apparent precipitating factor.

to such a point that tracheotomy is required. tuberculosis frequently develops, and eventually the patient, still leprosy, succumbs to tuberculosis (in nearly half the cases) or renal disease (in about one sixth of cases) or some other

condition. In a small proportion of cases, apparently without any constant relation to treatment, the lesions slowly subside and eventually become poor or even lacking in acid-fast bacilli, leaving only the residual neurologic changes, such a patient is sometimes said to have a "secondary neural" case. This process, which is tantamount to recovery, is rare even in cases of long standing and exceedingly rare in earlier cases. Its occurrence casts some doubt on the validity of the original classification of the case, as will be brought out under the heading of the "Tuberculoid Reaction." Hopkins and Faget's figures<sup>5</sup> are eloquent in this regard. Of 537 cases of lepromatous leprosy in their series, only 28 patients, 5 per cent, could be listed as "discharged, disease arrested, not (yet) readmitted." Thirty-one per cent had died.

The disposition of patients with leprosy of the lepromatous type is always the same institutionalization. These patients are like patients with "open" cases of tuberculosis from the standpoint of public health. They are the "infectious" cases of leprosy. The word is enclosed in quotation marks because the infectiousness of leprosy, even in this form, is slight, at least for most adults. Marital transmission of the disease, for example, is rare, Norman Sloan, Physician in Charge of Kalaupapa Settlement on the Island of Molokai in Hawaii, says that not one of the nearly 400 patients now under his care is suspected of having acquired the disease from a spouse, and the recent report from Carville by Hopkins and Faget<sup>5</sup> listed only 2 instances out of over 700 cases in which evidence of leprosy in a patient had developed following marriage to a leprosy person. It is believed, however, that children are much more susceptible than adults, and in any case, in the light or rather the darkness of the present state of knowledge regarding the transmission of the disease, one cannot do otherwise than isolate, in leprosaria, all patients known to have lepromatous leprosy.

#### "NEURAL" LEPROSY

"Neural" leprosy is that form of the disease which was once known as *leuce Graecorum*. Bateman<sup>1</sup> cites Celsus, Aetius, Aeginet and Actuarius as clearly describing a pale color and cutaneous anesthesia as the leading symptoms of a disorder under this name. He also cites Avicenna and Alsaharavius to the effect that *leuce* "possessed an affinity with" the *elephantiasis* of the Greeks. More recent synonyms for this form of leprosy are "macular," "anesthetic" or "maculoanesthetic" leprosy. The term "neural" has been official since 1931 when it was adopted at the Leonard Wood Memorial Confer-

ence on leprosy, in Manila.<sup>7</sup> It was officially redefined in March 1938 at the First International Congress on Leprosy, in Cairo, as follows:

*Neural (N) type*—All cases of the "benign" form of leprosy, with disturbances of polyneuritic nature (i.e., alterations of peripheral sensation, trophic disturbances, atrophies and paralyses, and their sequelae), or *macules of nonlepromatous nature* [italics mine] (i.e., leprides, usually with localized sensory disturbances), or both. These cases give evidence of relative resistance to the infection, are of relatively good prognosis as regards life, although mutilation may take place, and usually react positively to leprolin (*sic*).<sup>8</sup> Bacteriologically the skin lesions are typically but not invariably found negative by standard methods of examination, though the nasal mucosa may be found positive. Many of these lesions are histologically of tuberculoid nature.

"Neural" leprosy is therefore by no means synonymous with "nerve" leprosy, most modern textbooks to the contrary notwithstanding. The word is enclosed in quotation marks to remind the reader that this is the case. "Neural" leprosy involves both skin and nerves, as well as lymph nodes and perhaps testicles (Mitsuda<sup>2</sup>). The term "neural" is not only inapt, but an important source of serious confusion. Pardo-Castello<sup>10</sup> and Tilden and I<sup>11</sup> have suggested its abandonment and the adoption of "tuberculoid" in its place. The additional "simple inflammatory" category suggested by Pardo-Castello seems necessary for certain lesions, but I am not convinced that it is necessary for any cases, of the disease. It seems probable that a sufficiently thorough search would reveal tuberculoid histologic changes somewhere in virtually every case of this so-called "neural" type of leprosy.

"Neural" leprosy is characterized, then, by "disturbances of polyneuritic nature." So, however, is lepromatous leprosy. This feature is valueless in distinguishing between the two forms of the disease, except in one single respect: the distribution of the sensory disturbances in "neural" leprosy is likely to correspond at least in part to the extent of the cutaneous lesions.

7 Wade, H. W. A Proposed Revision of the Memorial Conference Classification of Leprosy, *Am J Trop Med* **17** 773 (Nov) 1937.

8 "Lepromin" is meant. This was an error in terminology which was subsequently explained and corrected.

9 First International Congress on Leprosy, *Internat J Leprosy* **6** 377 (July-Sept) 1938.

10 Pardo-Castello, V., and Tiant, F. R. Leprosy, *J A M A* **121** 1264 (April 17) 1943.

11 Tilden, I. L., and Arnold, H. L., Jr. The Two Kinds of Leprosy: Lepromatous and Tuberculoid, *Proc Staff Meet Clin, Honolulu* **10** 91 (Sept) 1944. Arnold, H. L., Jr., and Tilden, I. L. The Classification and Nomenclature of Leprosy, with Suggestions for the Simplification of Both, *Ann Int Med* **23** 65 (July) 1945.

themselves This is, as has already been stated, seldom true of lepromatous lesions To put it more explicitly, a hypopigmented macule—a lesion characteristic of “neural” leprosy—is often found to be anhidrotic and anesthetic to heat or cold or both Almost invariably, it also presents loss of the “axon reflex” a dermatographic wheal, or a histamine wheal, will manifest no surrounding erythema (flare) within the hypopigmented area The same statements are true of the elevated, granulomatous, frequently annular plaques which also characterize this form of leprosy

Secondly, “neural” leprosy is characterized by “macules of nonlepromatous nature (i e, leprides )” They are dealing here with “macules” in the leprologic sense, not the dermatologic sense In this usage a “macule” or lepride is a circumscribed lesion, usually hypopigmented (fig 3), not infrequently erythematous and infiltrated and elevated, and when elevated often annular in configuration (fig 4)



Fig 3 (case 2) —Hypopigmented, thermally anesthetic “simple macules” of “neural” leprosy

Thirdly, these lesions are nonlepromatous i e, they are typically poor or lacking in acid-fast bacilli “by standard methods of examination” This refers to the search for bacilli in thick smears of serum obtained from the cutaneous lesions by Wade’s “scraped incision” method The point of a scalpel or the corner of a safety razor blade is used to make a linear incision perpendicular to the surface of the skin and about 3 mm deep, and then the blade is rotated so that its edge scrapes one surface of this incision, removing a droplet of serum and a few cells This is deposited (not smeared) on a slide,

allowed to dry, fixed, stained and examined This procedure almost invariably serves to demonstrate abundant bacilli in lepromatous cases, but usually shows very few, or more often no, bacilli in “neural” cases An important exception to this rule is occasionally encountered the so-called tuberculoid reaction This is characterized clinically by little more than an apparent aggravation of existing lesions, some-



Fig 4—Typical elevated annular tuberculoid “macule” of “neural” leprosy The central portion, characteristically, was anesthetic Biopsy scar in upper part of lesion

times acute enough to produce superficial ulceration of them There is typically little or no fever, and erythema multiforme does not occur Bacilli, however, may be present in the lesions over a period of weeks or months, and it is possible for patients to be erroneously classified as lepromatous during this bacteriologically positive phase

The fourth characteristic of “neural” leprosy is that “many of these lesions are histologically of tuberculoid type” It has been shown repeatedly by Wade,<sup>12</sup> Lowe,<sup>13</sup> and many others,<sup>14</sup> and

12 Wade, H W, and Rodriguez, J N Borderline Tuberculoid Leprosy, *Internat J Leprosy* 8 307 (July-Sept) 1940, The Skin Lesions of Neural Leprosy II Observations in Cebu, *ibid* 5 1 (Jan-March) 1937 Wade, H W, and Fraser, N D The Skin Lesions of Neural Leprosy III Observations in China, *ibid* 5 285 (July-Sept) 1937 Wade, H W, Cochrane, R G, and Raj, M P The Skin Lesions of Neural Leprosy IV Observations in Madras, South India, *ibid* 5 437 (Oct-Dec) 1937 Wade, H W, de Simon, D S, and Fernando, A C The Skin Lesions of Neural Leprosy V Observations in Ceylon, *ibid* 6 199 (April-June) 1938



has been found to be true in Hawaii, that epithelioid cell tubercles with lymphocytic infiltration are regularly found in cases of "neural" leprosy when the lesions show any perceptible infiltration, and sometimes even when they do not. These tubercles are rather sharply circumscribed, and are generally less closely packed together than is the case in Besnier-Boeck-Schaumann's sarcoidosis, which they otherwise closely simulate (fig 5). They rarely show any trace of necrosis when they occur in the skin, but in nerve trunks caseation necrosis occurs frequently. Acid-fast bacilli may be found in them, in small numbers and after prolonged

in adults, and less often in children, who do not have the disease. It is believed that such a reaction is seen more frequently in countries where leprosy is endemic. The positive reaction consists, as has been stated, of an infiltrated red papule which takes two to three weeks to develop, and may ulcerate. Histologically, the mature reaction closely resembles the picture of reacting tuberculoid leprosy, foci of epithelioid cells occurring among and around the myriads of injected (dead) *Mycobacterium leprae*.

Positive reactions to serologic tests of the blood for syphilis probably occur in "neural" leprosy in the absence of syphilis, but the evi-

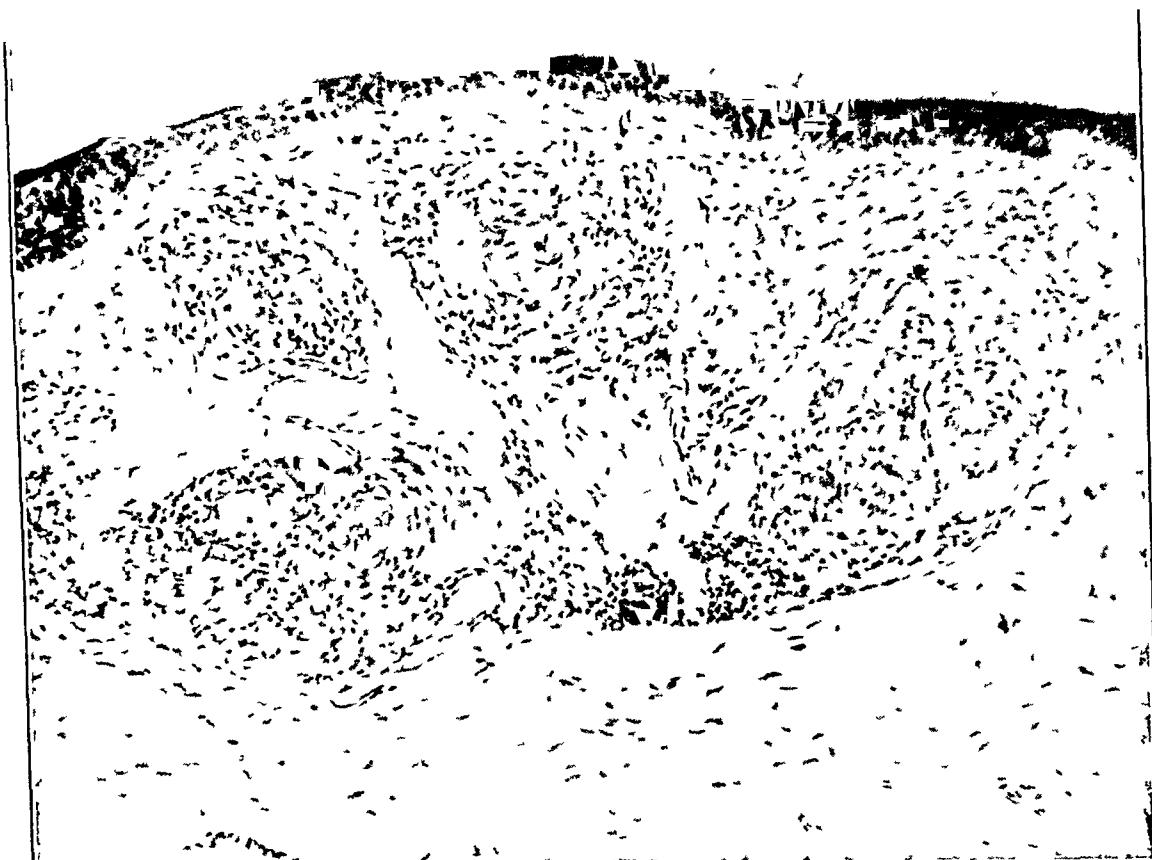


Fig 5—Four typical noncaseating epithelioid-cell tubercles of "neural" leprosy of "tuberculoid" subtype. Giant cell in the lower left hand tubercle. The superficial similarity to sarcoidosis is apparent. Hematoxylin and eosin,  $\times 130$ .

search, almost invariably, even in cases in which repeated examinations of material obtained by the scraped incision method have failed to demonstrate the organism (fig 6).

The skin of patients with "neural" leprosy regularly reacts positively to injected lepromin. This positive reaction does not indicate the presence of leprosy, it is also found frequently

13 Lowe, J. A Study of Macules in Nerve Leprosy with Particular Reference to the "Tuberculoid" Macule, *Internat J Leprosy* 5 181 (April-June) 1937.

14 Ermakova, N. The Histopathology of Simple Leproids, *Internat J Leprosy* 7 495 (Oct-Dec) 1939.  
Stein, A. A. Tuberculoid Changes in Leprosy, *ibid* 8 41 (Jan-March) 1940.  
Saunders, G. M., and Giffen, H. K. The Skin Lesions of Neural Leprosy in the Virgin Islands of the United States, *ibid* 10 38 (Jan-March) 1942.

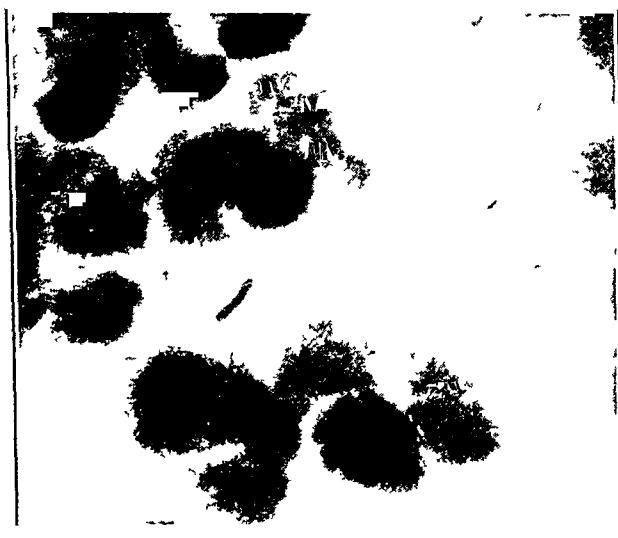


Fig 6 (case 2)—Solitary *Mycobacterium leprae* in one of the macules shown in figure 3. Fite's fuchsin-formaldehyde,  $\times 1,800$ .

dence is less conclusive than is the case with lepromatous leprosy. Hopkins and Faget<sup>5</sup> found 11 per cent positive Kolmer Wassermann reactions in 175 "neural" cases, and 13 per cent positive Kahn reactions. Badger,<sup>6</sup> interestingly, found no difference in this regard between cases with cutaneous and those with neural sites of involvement.

The prognosis of "neural" leprosy is good for arrest and even fairly good for recovery. It is not generally believed that treatment, except perhaps for the good effect of rest and improved diet implicit in a hospital regimen, has any observable effect in this regard. Improvement, like aggravation of lesions, seems to be spontaneous. It is believed to occur as a result of the patient's immune reaction to the presence of the bacillus, as manifested in the positive reaction to the lepromin test. It is by no means unusual to see a patient with a few tuberculoid "macules" begin to improve within a year or so of their initial appearance, and recover almost completely, except perhaps for residual flushing or dyspigmentation of the area, within another year. The associated anesthesia may disappear as well, though more advanced neurologic changes, such as muscular atrophy or contractures, seldom disappear entirely. In Hopkins and Faget's series of 186 "neural" cases (of which 31 were classified separately as tuberculoid), 56 per cent of the patients were listed as discharged and not yet readmitted in relapse, and only 8 of a total of 110 so discharged had had to be so readmitted.

The disposition of cases of "neural" leprosy is not always the same. They do not all require institutionalization. It is probable that some official body should assume the responsibility for deciding that hospitalization is not required in any given case. It is the practice in Hawaii to hospitalize all patients with acid-fast bacilli demonstrated by the scraped incision method, and also to hospitalize most patients in whom the disease seems clinically active, i. e., those who have elevated, erythematous, infiltrated or ulcerated lesions. The latter are hospitalized not so much as menaces to the public health, as for their own good. It is felt that rest and adequately supervised diet are helpful in accelerating the onset of the spontaneous arrest.

#### DIFFERENTIAL DIAGNOSIS

Assuming that the diagnosis of leprosy has been arrived at or at least strongly suspected, how is the distinction to be made, in office or clinic practice, between lepromatous and "neural" types?

*Dermatologic Differentiation*—The distinction may often be made with reasonable assurance on the basis of inspection alone. This does *not* mean inspection with a view to deciding whether leprosy is primarily neurologic or primarily cutaneous, such a distinction is utterly valueless. Notwithstanding this fact, it has been widely employed, often by men who should and do know better. It must be kept clearly in mind at all times that leprosy of nerves, like leprosy of skin, may be either lepromatous or "neural" in type, it is not the *tissue* that has the disease, but the *entire patient*, that must be considered.

The oldest clinical evidence is perhaps the best clinical evidence. Has the patient hypopigmented macules, or has he not? Hypopigmented macules are frequently present in "neural" leprosy, and they are seldom present in lepromatous cases. If this test fails, look for an annular configuration of the lesions. The lepromas of lepromatous leprosy are seldom annular, while the tuberculoid "macules" of "neural" leprosy are frequently so. Positive evidence of the lepromatous nature of a lesion does not rest on nearly as secure ground. Striking diffuse or nodular infiltration of the ears or face is highly suggestive of lepromatous leprosy. It is well, however, to make only a tentative decision on the basis of inspection of the patient, in making this differentiation experience is indeed fallacious and judgment difficult.

*Neurologic Differentiation*—One must remember that the absence, or presence, or extent, of evidence of nerve damage has no bearing whatever on the differentiation of lepromatous from "neural" leprosy. The important point here is to decide whether the visible cutaneous lesions tend to coincide in extent with the demonstrable anhidrosis, or anesthesia, or loss of the flare about the histamine wheal. If this is the case—if nerve damage can be demonstrated just within the border of the hypopigmented or annular lesion—it is highly probable that the case is a "neural" one. If this is not the case, the evidence is slightly, though only very slightly, in favor of the lepromatous form of the disease.

*Bacteriologic Differentiation*—Bacteriologic examination, in the majority of cases, will make the distinction reasonably secure if bacilli are scanty or absent. Such a finding is strongly suggestive of the "neural" type of the disease. If bacilli are fairly numerous, it means that the patient has either lepromatous leprosy or (less probably) "neural" leprosy in a transitory tuberculoid reaction. Only a series of examinations over weeks or months will permit evaluation of such a case on bacteriologic grounds, and some-

times this is the only way of arriving at the differentiation. This examination is readily made in the office by Wade's scraped incision method, as already described. A proper preparation should contain few red blood cells, and should show at least one or two lymphocytes or histiocytes in almost every oil immersion field. The usual Ziehl-Neelsen stain is perfectly satisfactory if decolorization is not overdone.

A special word of warning should be inserted here. Nasal scrapings or smears are worthless at best, and misleading at worst, in the diagnosis of leprosy or the differential diagnosis of the two types of the disease. It is perfectly true that lepromatous lesions of the nasal mucous membrane are fairly common, and that *Myco leprae* can be found with ease in scrapings from such lesions. But it is also true that acid-fast diphtheroid bacilli morphologically indistinguishable from *Myco leprae* may be found in either the normal or the leprosy nasal mucous membrane, and conversely, that a leprosy patient may fail to show acid-fast bacilli of any sort in nasal scrapings. Eskey,<sup>15</sup> at Kalihı Hospital in Honolulu, was able to cultivate acid-fast bacilli repeatedly from nasal scrapings taken from leprosy patients. The two conclusions are inescapable: (1) The presence of acid-fast bacilli in smears of nasal scrapings does not mean that the patient has leprosy, and (2) the absence of such bacilli does not mean the absence of leprosy. Controlling the smears with cultures will not help, because negative cultures would be inconclusive and positive cultures would not exclude the possibility that *Myco leprae* was also present. The examination of nasal smears or scrapings has, therefore, no place in the diagnosis of leprosy or in the differentiation of the two types.

*Histologic Differentiation* The fourth step in evaluation when leprosy is suspected is biopsy. This should be made in every case. In the bacteriologically positive cases it is needed in order to distinguish, if possible, between lepromatous leprosy and reacting tuberculoid leprosy, in the bacteriologically negative cases it is desirable in order to establish the presence or absence of tuberculoid histologic changes, and it is useful in order to furnish (as it usually will) bacteriologic evidence that the lesion is actually leprosy. In my experience histologic examination of sections stained by Fite's fuchsin-formaldehyde method has repeatedly served to demonstrate occasional acid-fast bacilli in lesions in which no bacilli could be found by the scraped incision procedure, and in which in some cases the histologic changes were nonspecific.

<sup>15</sup> Eskey, C. R. Personal communication to the author.

*Biologic Differentiation* These four procedures will serve to establish the differential diagnosis in most cases. In the event that doubt still exists, however, a lepromin test may be performed. In my limited experience with this test, the results have not been entirely satisfactory, possibly for technical reasons, but there can be no doubt that in general it will give a strongly positive reaction in the great majority of "neural" cases and a negative reaction in virtually all lepromatous cases. In a nonleprosy person, of course, either response may be obtained. It has two major drawbacks. The material for performing it is not commercially available, and the test requires from two to four weeks for evaluation.

#### REPORT OF CASES

**CASE 1**—A Hawaiian girl aged 13 was referred to the Clinic of the Board of Hospitals and Settlement as suspected of having leprosy because of a deep red, sharply outlined, palm-sized macule on the right forearm and the finding of acid-fast bacilli in nasal scrapings. Examination disclosed no other lesions than the one mentioned, which had the appearance of a port wine hemangioma and was said to have been present since infancy. A thorough neurologic examination disclosed no palpable nerve trunks except the ulnar nerves, which were equal and normal in size, there was no evidence of muscular weakness, atrophy or contractures, and there was no anesthesia to heat or cold anywhere on the cutaneous surface. The nasal scrapings were repeated as a courtesy to the referring physician, and no acid-fast bacilli were found in them. The diagnosis was port wine hemangioma with no evidence of leprosy. The patient was officially certified as not leprosy.

*Comment* This case provides a classic example of the inadvisability of performing nasal scrapings on patients suspected of having leprosy. The "positive" finding here was the only feature of the case that even seemed to justify the suspicion of leprosy. The complete absence of thermal anesthesia in a patient whose only cutaneous lesion was of many years' standing excludes the possibility of leprosy with reasonable certainty.

**CASE 2**—A part-Hawaiian woman aged 23, a housewife, was referred to the Clinic of the Board of Hospitals and Settlement as suspected of having leprosy because of anesthesia of the left foot. A biopsy had been made from the anesthetic region, and had been reported as showing only minimal, banal, perivascular inflammatory infiltration, without acid-fast bacilli.

Examination disclosed a healthy-looking young woman who presented no lesions of the skin except half a dozen sharply outlined hypopigmented macules, without erythema or infiltration, on the forearms (fig 3). Most of the macules were anesthetic to heat and cold, though not to light touch. The left foot, from the ankle joint distally, was anesthetic to heat and cold, light touch and pinprick. No abnormal nerve trunks were noted in the neck or arms, but the left posterior tibial and sural nerves

were thickened and tender from the point where they passed beneath the malleoli to a point several centimeters distally. No acid-fast bacilli were found in fluid obtained from scraped incisions in the anesthetic portion of the foot and in two of the macules.

Biopsy from the border of one of the macules showed only moderate perivascular lymphocytic and histiocytic infiltration, but acid-fast stains disclosed half a dozen widely scattered individual acid-fast bacilli (fig 6). A routine nasal scraping disclosed abundant acid-fast bacilli morphologically indistinguishable from *Mycobacterium leprae*. The nasal scrapings were repeated forty-eight hours later on each side of the nasal septum, and no acid-fast bacilli could be found in either smear.

The diagnosis was leprosy, "neural" type, subtypes simple macular and anesthetic, minimal degree (Ns 1, Na 1). The patient was officially certified as leprosy and granted immediate temporary release (parole) status, to report monthly for observation.

*Comment* This case well exemplifies the futility of using nasal scrapings as a means of distinguishing between lepromatous and "neural" leprosy. It seems highly improbable that a bacteriologically positive leprosy lesion of the nasal mucous membrane would have healed or become bacteriologically negative within forty-eight hours. If the bacilli found in the first smear had been *M. leprae*, they should still have been readily demonstrable two days later. The most likely explanation seems to be that they were (like the organisms in case 1) nonpathogenic diphtheroid bacilli, only temporarily present. Confusion would have been avoided and no advantage lost if the nasal scrapings had not been performed.

Attention is also invited to the importance of biopsy and acid-fast stains as a means of demonstrating rare bacilli even in relatively early cutaneous lesions of "neural" leprosy.

**CASE 3**—A part-Hawaiian girl aged 19 was referred to my office because of a numb area on her right calf, present for about four months. Examination disclosed no visible, and no readily palpable, abnormality. Repeated deep palpation at right angles to the border of the anesthetic area revealed just a suspicion of infiltration in that region. A deep biopsy showed replacement of nerve trunks in the hypoderm by characteristic epithelioid cell tubercles. Prolonged search of several sections finally revealed rare acid-fast bacilli in a few of these tubercles (fig 7). The diagnosis was leprosy, "neural" type, subtypes anesthetic and tuberculoid, minimal degree (Na 1, Nt 1). Because of the absence of cutaneous lesions, the patient was not officially certified at this time, but merely kept under unofficial observation.

Seven months later, the anesthetic area underwent a typical tuberculoid reaction, with the development of a reddened, elevated, infiltrated tuberculoid annule surrounding it, and moderate spread. The patient was officially certified as leprosy at this time, and was granted immediate temporary release, with instructions to report monthly for observation. In the ensuing year the lesion slowly subsided and the area of anesthesia

diminished, so that at present the patient shows only faint pinkness and scaliness along the border of the original palm-sized area of anesthesia.

*Comment* This case is of interest primarily because it is unusual to see tuberculoid leprosy of the skin (or more exactly, of the smaller branches of cutaneous nerves) without any visible lesion. The case also well illustrates the great diagnostic value of biopsy even with scanty clinical evidence of abnormalities.

**CASE 4**—A Japanese man aged 26 was referred to the Clinic of the Board of Hospitals and Settlement as suspected of having leprosy. Examination disclosed a young man with total alopecia of brows and lashes, left facial weakness, more evident about the eye than in the lower portion of the face, weakness, atrophy and moderate contracture of the left hand and forearm, and tactile anesthesia of both legs up to about the knees, of the entire left arm and of portions of the face. This process was said to have begun six years before with diffuse swelling of the face, diagnosed as nephritis by the family physician, shortly afterward, the patient recognized it as leprosy and thereafter avoided doctors. In recent months, some cutaneous lesions had appeared. There were dull redness and thickening of the helixes of both ears, sharply elevated, dull red, rubbery firm nodules were present on both elbows, and there was a faint pink eruption of small papules on the trunk, especially anteriorly. Bacteriologic examination of serum obtained from lesions on the ear and chest revealed abundant acid-fast bacilli in clumps and globi. Biopsy was not done. A lepromin test, a few weeks later, elicited only faint brown pigmentation in an area 3 mm in diameter at the end of three weeks, and was interpreted as negative. The diagnosis was leprosy, lepromatous, moderately advanced (L 2). The patient was officially certified and committed to Kalihni Hospital for isolation and observation.

*Comment*—The value of this case lies chiefly in its clear demonstration of the uselessness of attempting to differentiate lepromatous from "neural" leprosy by an evaluation of the relative degrees of involvement of the nerves and of the cutaneous tissue. Here is a patient with neurologic changes—alopecia, anesthesia, muscular weakness, atrophy and contracture of moderately advanced degree, and only slight cutaneous changes, who nevertheless, as shown by bacteriologic examination, the negative lepromin test and his subsequent steady downhill course, has not the "neural" but the lepromatous form of the disease.

This is the type of case that would be classified in some clinics as "mixed" leprosy (L 2, N 2), because the neurologic involvement is moderately conspicuous. The utilization of this term to designate a separate type of the disease, besides being contrary to the explicitly expressed intention of the Cairo Congress,<sup>9</sup> serves only to confuse the issue, because it so clearly implies a mixture of the two types of the disease instead of, as is actually the case, a mixture of the two

major sites of involvement. Moreover, it tends to divert attention from the important fact that virtually every case of lepromatous leprosy has at least some degree of involvement of nerves as well as of skin. The term "mixed" leprosy should be abandoned altogether.

neous lesion. He presented a profuse eruption of irregularly oval, sharply outlined, hypopigmented macules scattered over the trunk, several of these on the lower part of the back and buttocks were surrounded by an elevated, reddened, infiltrated annulus varying from 1 to 3 cm in width. All of the larger macules and a few of the smaller ones presented thermal anesthesia, none



Fig 7 (case 3) —A, replacement of nerve twigs in the hypoderm by epithelioid cell tubercles. Hematoxylin and eosin,  $\times 40$ . B, one of the tubercles from A. Hematoxylin and eosin,  $\times 300$ . C, solitary *Mycobacterium leprae* in one of the tubercles. Fite's fuchsin-formaldehyde,  $\times 1,800$ .

CASE 5—A Portuguese man aged 21 was referred to the Clinic of the Board of Hospitals and Settlement as suspected of having leprosy because of a hypopigmented macular eruption of four months' duration and the finding of acid-fast bacilli in serum obtained from a cuta-

was anesthetic to touch, nor was tactile anesthesia demonstrable anywhere on his skin. There was minimal weakness of the lower part of the left side of the face and slight interosseous atrophy in the left hand. Both hands were cyanotic when dependent, and slightly

swollen The anterior divisions of both great auricular nerves were visible and easily palpable, and the left was nearly twice the diameter of the right The right ulnar nerve was almost twice as thick as the left, and was rounded, firm and cordlike, the left seemed thicker than normal

Smears of serum obtained from an infiltrated annulus on the buttock revealed only 2 acid-fast bacilli after prolonged search Biopsy from the same lesion showed sharply outlined foci of granulomatous infiltration scattered throughout the corium and hypoderm, these were composed largely of round and spindle-shaped cells with foamy cytoplasm, and most of the foci contained from a few to 40 or 50 acid-fast bacilli The distribution of the infiltrate was suggestive of tuberculoid leprosy, but its character was more in keeping with lepromatous leprosy A lepromin test was made, and at the end of three weeks resulted in the formation of a brownish, slightly scaly papule 2 mm in diameter, barely elevated above the surface The test was interpreted as negative The diagnosis was leprosy, type indeterminate The patient was officially certified and committed to Kalahe Hospital for observation

*Comment* This case presents one clinical feature of special interest and significance there was readily demonstrable and extensive thermal anesthesia, but no demonstrable tactile anesthesia When anesthesia to light touch can be demonstrated, leprosy may well be suspected, but when it cannot be demonstrated, thermal anesthesia should always be looked for before concluding that the sensory examination is "negative" It is decidedly commonplace, some texts to the contrary notwithstanding, to see this complete dissociation of thermal and tactile sensation

The classification of this case poses a puzzling problem Clinically, because of the hypopigmented and anesthetic macules and the annular lesions, it should be classified as a "neural" case, of all three subtypes—simple macular, anesthetic and tuberculoid (Na 1, Ns 1, Nt 1) Histologically it seems lepromatous, though per-

haps the histologic structure could be explained on the basis of tuberculoid leprosy in a bacteriologically positive reaction Biologically—by the lepromin test—the case also seems to be of the lepromatous type A period of observation seems necessary before arriving at a final decision

#### SUMMARY

Lepromatous leprosy is characterized by granulomatous lesions of the skin, nerves, lymph nodes and viscera, abundant bacilli, variable neurologic changes, a negative reaction to the lepromin test, and a progressive downhill course

"Neural" leprosy is characterized by hypopigmented cutaneous lesions and sarcoid-like lesions of the skin, nerves and lymph nodes, scanty bacilli (except during reactions), variable neurologic changes, a positive reaction to the lepromin test, and a tendency to spontaneous arrest and healing

These forms may usually be distinguished in practice by attention to the clinical appearance of lesions, by comparison of the distribution of sensory changes with that of changes in the skin, by search for bacilli in tissue fluid, by biopsy and by the lepromin test

The distinction should always be made, when possible, because it permits a prognosis to be made, it guides the physician in his disposition of the case, it makes possible the evaluation of treatment, and—if it is favorable—it permits the physician to soften the blow when he informs the patient of the nature of the illness

Dr Irvin L. Tilden, of the Department of Pathology of The Clinic, Honolulu, made the histologic preparations, the clinical photographs and the photomicrographs, and assisted in the preparation of the portions of the paper dealing with histopathology

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# SANDALS, AND HYGIENE AND INFECTIONS OF THE FEET

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The high incidence of cutaneous diseases of the feet due to infection and hyperhidrosis among military personnel in tropical and summer temperate climates greatly interferes with the efficient performance of military functions. The extent and severity of such infection are not generally realized. Moreover, the problem in the tropics is not peculiar to the army, and return of infected personnel may bring it into sharp focus in this country. Various estimates give the percentage of Army and Navy personnel free from clinical evidence of infection of the feet at only 20 per cent, estimates for civilian industrial populations show only a slightly better situation. Callaway<sup>1</sup> has stated that "no effective fungicide is yet available which does not have certain disadvantages. . . most prescribed remedies depend not on their fungicidal action but on keratolytic action". Hopkins<sup>1</sup> pointed out that "almost any agent that is fungistatic and not too irritating to the skin shows some curative effect". The great number of different treatments that have been proposed is in itself evidence that a specific treatment is not at hand.

An examination of dispensary records in the Army Air Forces Proving Ground Command revealed that 30 per cent of the outpatients for the months from May through October came because of infections of the feet. A similar or more serious situation is common in other commands in hot, humid climates. On the assumption that aeration was essential to hygiene of the feet, a preliminary trial with twenty pairs of open-toed sandals for everyday wear was conducted at Eglin Field. After reviewing the favorable effects on hygiene of the feet which this preliminary test showed, the Air Surgeon requested that the Army Air Forces Proving Ground Command ascertain experimentally the

value of sandals in reducing infections of the feet. A controlled test with over 2,000 men was conducted for a two month period. The aid and advice of the Surgeon, Colonel J. A. Schindler, and the interest and cooperation of the entire Command made it possible to carry the test to conclusive results.

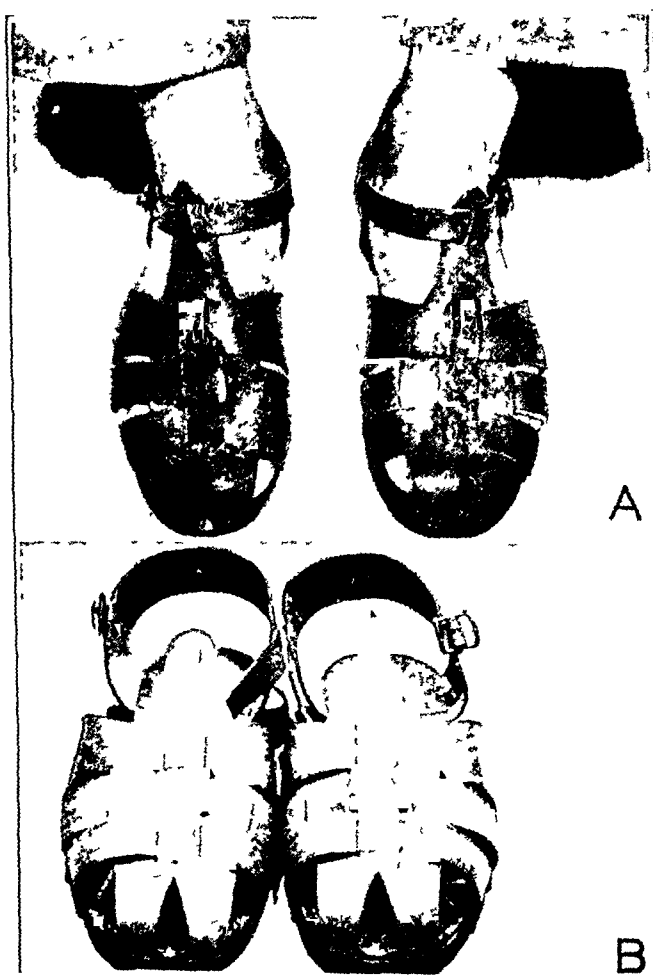


Fig 1—A, sandals were commonly worn without socks. B, sandals were constructed with leather sole and upper, and rubber heel, closure was effected by a single leather thong and metal buckle.

Sandals of the type shown in figure 1 were issued during the week of May 15, 1944 to 1,200 men after allocation to various components of the Command, different groups were examined on successive days of that week. In some

From the Physiological Projects Section, Proof Division, Army Air Forces Proving Ground Command  
1. Personal communication to the authors.



groups sandals were issued to every man examined, in some the men were examined but no sandals were issued, while in the remaining groups every other man received sandals. These procedures were adopted to make the distribution statistically significant.

Medical examiners classified the clinical state of infection of the feet into one of five classes,<sup>2</sup> from (I) negative to (V) very severe. Of 2,100 men examined during the week of May 15 (1,200 experimental, 900 control), only 19 per cent showed no visible signs of infection and 23 per cent of the men (in classes IV and V) had infections severe enough to be of medical concern. Reexaminations similar to the initial examination were held at the end of the first and second months. During this time, with a few exceptions, the men who had been issued sandals wore them to the exclusion of other types of footwear, a large number of the men wore sandals without socks. No type of treatment was given to either control or experimental groups during the period of the test.

A comparison of the incidence of infection of the feet at the beginning of the test and at the end of the second month, at which time the test was terminated, is presented in table 1 and figure 2. The figures show that the condition of wearers of sandals improved greatly while that of the control group deteriorated rapidly as the

cern, among the group wearing shoes 28 per cent were in a serious condition.

Colored photographs were taken of the feet of about 75 men with an initially severe infection (class IV or V). Subsequent pictures<sup>3</sup> in color were taken of the same men at each of the two monthly reexaminations. Subjects were photographed in the group wearing sandals or in the control group.

Questionnaires were given to all men at the initial examination and to those who wore

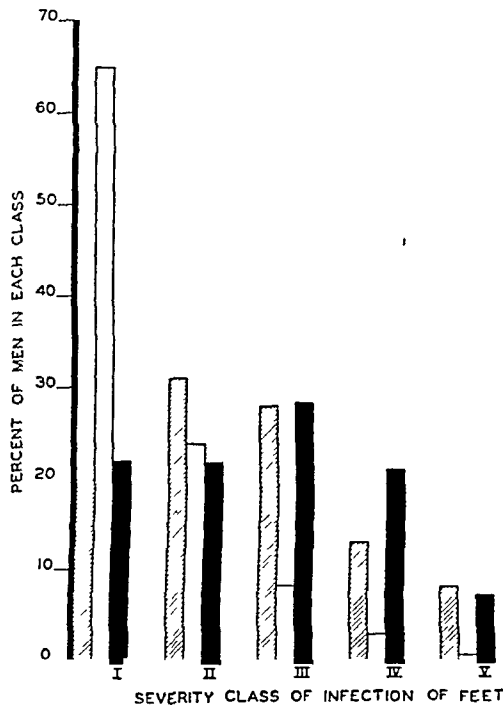


Fig 2—Summary of infections of feet at beginning and end of sandal test. The cross-hatched columns indicate results of initial examination, the white columns, results in group wearing sandals, and black columns, results in group not wearing sandals. The class of severity of infection is indicated thus: I, normal, II, mild, III, moderate, IV, severe, and V, very severe.

TABLE 1—Incidence of Infection of Feet at Beginning of Test and at End of Second Month

| Severity Class  | Initial Examination |                   | Final Examination |                   |                 |                   |
|-----------------|---------------------|-------------------|-------------------|-------------------|-----------------|-------------------|
|                 | No of Men           | Per Cent of Total | Sandal Group      |                   | Nonsandal Group |                   |
|                 |                     |                   | No of Men         | Per Cent of Total | No of Men       | Per Cent of Total |
| I (negative)    | 397                 | 19                | 373               | 65                | 120             | 22                |
| II (mild)       | 628                 | 29                | 134               | 23.5              | 121             | 22                |
| III (moderate)  | 605                 | 29                | 45                | 8                 | 154             | 28                |
| IV (severe)     | 283                 | 13.5              | 16                | 3                 | 114             | 21                |
| V (very severe) | 207                 | 9.5               | 2                 | 0.5               | 40              | 7                 |

summer heat and humidity increased. Only 3.5 per cent of those who wore sandals were seriously affected at the end of the two month period, and with this group the disease had practically ceased to be a problem of medical con-

2. Classes were defined as follows: (I) Negative; (II) Mild—mild or slight scaling, redness, closed, initial, or slight fissures; (III) Moderate—moderate scaling, redness, mild to moderate fissures, slight sodden patches, mild tissue changes; (IV) Severe—severe scaling, sodden patches, fissures, tissue changes; (V) Very severe—marked eczematoid condition, severely aggravated condition, very severe sodden patches and fissures, extreme vesiculation, marked tissue changes.

sandals at the first reexamination. From the answers it was learned that the sandals were extremely popular with the men, 88 per cent of the wearers liked them and 84 per cent preferred sandals to low quarter shoes for wear during the hot months, while 87 per cent preferred them to service shoes. While on the first questionnaire 99 per cent of the men said their feet perspired noticeably while wearing shoes during the hot months, 87 per cent of those who wore sandals said at the end of one month that their feet did not get sweaty.

A method was selected to express how much better or how much worse a man became during

3. Two comparison sets appeared in color in Nicker- son, W. J., Irving, L., and Mehmert, H. E. Effect of Wearing Sandals in Reducing Foot Infections, *Air Surgeons' Bull.* 2:120-121, 1945.

the course of the test One man improving one class constitutes one positive unit, one man deteriorating one class constitutes one negative unit On the basis of the initial and final examinations, the overall figures are given in table 2 (it was possible to get back 1,119 of the men originally examined for the second reexamination)

TABLE 2—*Severity Class of Changes During Test at End of Second Month*

| Group with Sandals              |                                  | Control                         |                                   |
|---------------------------------|----------------------------------|---------------------------------|-----------------------------------|
| 26/570 worse 4% (—32 units)     |                                  | 217/549 worse 40% (—307 units)  |                                   |
| 165/570 same 29%                |                                  | 185/549 same 34%                |                                   |
| 379/570 better 67% (+715 units) |                                  | 147/549 better 26% (+193 units) |                                   |
| 683 + units                     |                                  | 114 — units                     |                                   |
| 570 men                         | = 1.2 class improvements per man | 549 men                         | = 0.2 class deterioration per man |

At the end of the first month of the test it was found that the group wearing sandals had improved an average of 1 class per man while the control group had deteriorated  $\frac{1}{5}$  class per man At the end of the second month, as shown in table 2, the average change was 1.2 class improvements per man for the group wearing sandals and  $\frac{1}{5}$  class deterioration for the controls

It is significant that many men in the group wearing sandals, who initially had serious conditions of the feet which improved while they were wearing sandals, reverted to a serious condition if and when it became necessary for them again to wear shoes routinely In table 3 data on this point are presented for a group of 89 men

TABLE 3—*Condition After Wearing Sandals and After Again Wearing Shoes*

| First Month—Sandals                   |                                    |
|---------------------------------------|------------------------------------|
| 27/89 men or 30% worse (—41 units)    |                                    |
| 23/89 men or 26% no change            |                                    |
| 39/89 men or 44% improved (+65 units) |                                    |
| Plus 24 units                         |                                    |
| 89 men                                | = 0.25 units per man improvement   |
| Second Month—Wearing Shoes            |                                    |
| 55/89 men or 62% worse (—89 units)    |                                    |
| 19/89 men or 21% no change            |                                    |
| 15/89 men or 17% improved (+24 units) |                                    |
| Minus 65 units                        |                                    |
| 89 men                                | = 0.73 units per man deterioration |

whose sandals were no longer serviceable at the end of the first month of the test

It is noteworthy that only 1 case of trauma, preventable by wearing service shoes, was reported while the group of 1,200 men was wearing sandals during the two month period of the test This case was a first degree burn of a small area of one foot suffered by a welder

It was noted during the examinations that two general categories of conditions of the feet exist, they occur among those with the more severe cases and fall into our classes III, IV or V The first type may be called "sodden" and is characterized by extensive dead white, sodden areas at the base of toes where they may be tightly opposed, extensive and severe fissuring at the base of toes commonly accompanies this type, fungi can rarely be isolated from the lesions, but *Staphylococcus aureus* is frequently found The second type of condition can be called "vesicular" and is marked by the presence of numerous small vesicles with considerable itching as an accompaniment, this irritation frequently results in severe aggravation at the site due to scratching It was thought that the sandals might be having more effect on one of these types than on the other, so the data were analyzed with this in mind

TABLE 4—*Effect of Sandals on Sodden and on Vesiculative Condition of Feet*

| Sodden Type—First Monthly Reexamination       |                         |
|---|-------------------------|
| Sandal Group                                  | Control Group           |
| 14/235 or 6% worse                            | 46/142 or 32% worse     |
| 33/235 or 14% no change                       | 49/142 or 35% no change |
| 188/235 or 80% better                         | 47/142 or 33% better    |
| Vesiculative Type—First Monthly Reexamination |                         |
| Sandal Group                                  | Control Group           |
| 9/127 or 7% worse                             | 13/37 or 35% worse      |
| 26/127 or 21% no change                       | 14/37 or 38% no change  |
| 92/127 or 72% better                          | 10/37 or 27% better     |

As will be noted, there is no significant difference in the effect of wearing sandals on either type of infection both respond equally well

During the two month period of the test 16 men in the control group were admitted to the hospital for severe dermatitis or cellulitis of the feet, in the corresponding period only 1 man from the group wearing sandals was admitted for similar reasons The average stay was thirteen days in the hospital for these 17 men Thus two hundred and eight days in the hospital were chargeable to the 900 men wearing shoes while only thirteen days were used by the 1,200 men wearing sandals, a substantial economy of duty time and medical attention was effected by the use of sandals in these serious cases alone The 16 not wearing sandals who were hospitalized were issued sandals on being discharged from the hospital, it was estimated that the men were able to leave, on an average, five days earlier than if sandals could not have been issued

Thus it appears that by wearing sandals cutaneous diseases of the feet of the type observed can practically be removed as a cause for serious medical concern. In fact, in the experimental groups the incidence of infection of the feet was so low at the conclusion of the test as to suggest the possibility of eliminating the disease entirely from an organization if the general use of sandals as a prophylactic measure was occasionally supplemented by mild medicative treatment.

From what appears to be known, dermatophytosis seems only recently to have become the widespread problem that it is, and would seem to be one more on the growing list of "diseases of civilization."

Lewis and Hopper<sup>4</sup> state, "One of the factors thought to be important in predisposing toward fungus infections of the toes is the moisture

normally present or due to lack of drying after a bath or other conditions." It is known from many sources that moisture, in some form, is a prerequisite for germination of fungus spores and continuance of growth of the organisms. The results of the present study seem to afford ample confirmation of the view, held by many, and reflected in the statement from Lewis and Hopper, that evaporation of moisture from perspiration is of great importance in protecting the feet from infection.

It might be profitable to think that the value of sandals lies in the fact that they prevent the accumulation of sweat, and by aeration and free movement of toes favor a good cutaneous circulation, which is one of the best barriers against infection.

For part of the week of the second reexamination two observers for the National Research Council were present at this study. Dr J L Callaway, Duke University Hospital, and Dr J G Hopkins, Columbia College of Physicians and Surgeons. Dr Fred Wulsin and Lieut Col J R Scholtz gave advice and encouragement.

<sup>4</sup> Lewis, G M, and Hopper, M. An Introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc, 1939.

# THE ADRENAL GLANDS IN PEMPHIGUS VULGARIS

## REPORT OF SIX AUTOPSIES AND REVIEW OF THE LITERATURE

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Although the literature dealing with pemphigus is extensive, the greatest proportion relates to therapy or etiologic investigations, only a small fraction concerns itself with the pathology, pathophysiology or histochemistry of this disease. Biochemical changes were noted as far back as 1872, when Krieger<sup>1</sup> remarked on the absence of urinary chlorides in 1 case. In the last decade a great deal of study has been devoted to the changes in electrolyte metabolism.<sup>2</sup> This work, however, was of more or less academic interest until Talbott, Lever and Consolazio<sup>3</sup> called attention to the fact that the electrolyte pattern, particularly in cases of acute pemphigus, was almost identical with that observed in cases of acute adrenal insufficiency. The therapeutic consequences of these observations apparently mark a great step forward in the treatment of certain types of pemphigus. Goldman,<sup>4</sup> Goldzieher,<sup>5</sup> Gellis and Glass<sup>6</sup> and Talbott and others<sup>7</sup> have used adrenal cortex extracts or desoxycorticosterone acetate (with or without vitamin supple-

ments) and have induced remissions in a significant number of cases, in some instances permanent remission seems to have been obtained. In cases in which the disease eventually became refractory to cortex extracts there has been subsequent response to the synthetic sterol.<sup>4</sup>

In view of the characteristic electrolyte pattern that had been observed and in view of the promising therapeutic results that had been obtained on this basis, it appeared worth while to investigate the morbid anatomy of the adrenals in patients with pemphigus vulgaris. The present communication is the report of the observations in 6 cases coming to autopsy at New York City Hospital, Welfare Island, New York.

### REVIEW OF THE LITERATURE

Of the 105 autopsy reports in the literature, only a small proportion (as indicated in the table) contribute to this investigation. In 42 protocols, the adrenals are not mentioned at all. In 15 others, they are dismissed with the single word "normal." The misleading phrase "postmortem autolysis" seems to exclude an additional 8. In only 8 cases of the entire group are the adrenals described in detail, some data can be gleaned from 16 of the 37 cases in which they are inadequately described.

Two cases terminated in the patient's having Addison's disease. Tomlinson and Cameron<sup>8</sup> described the adrenal cortex as "almost entirely degenerated, with only occasional nests of cortical cells in the connective tissue stroma." The case of Becker<sup>9</sup> reported by Wells and others<sup>10</sup> appears to have been remarkably similar, the adrenal lesions were "typically those of Addi-

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1 Krieger, K. Ein Fall von Pemphigus Foliaceus, *Memorabilien, Heilbr* 17 531-540, 1872.

2 Cassact, E., and Micheleau, E. Sur deux cas de pemphigus traité par la dechloruration, *Arch gén de med* 1 129-140, 1906. Prakken, J. R. Weitere Untersuchungen über die erhöhte Ausscheidung von Chlor durch die Haut bei Pemphigus, *Acta dermat-venereol* 17.103-111 (April) 1936.

3 Talbott, J. H., Lever, W. F., and Consolazio, W. V. Metabolic Studies on Patients with Pemphigus, *J Invest Dermat* 3 31-68 (Feb) 1940.

4 Goldman, A., Markham, M. J., and Schaffer, A. I. Clinical Report of Treatment of Case of Pemphigus with Desoxycorticosterone Acetate, *J Clin Endocrinol* 2.343-344 (May) 1942.

5 Goldzieher, M. A. The Adrenal Glands in Health and Disease, Philadelphia, F. A. Davis Company, 1944, p. 680.

6 Gellis, S., and Glass, F. A. Pemphigus. Survey of One Hundred and Seventy Patients Admitted to Bellevue Hospital Between 1911 and 1941, *Arch Dermat & Syph* 44 321-336 (Sept) 1941.

7 Lever, W. F., and Talbott, J. H. Pemphigus. A Further Report on Chemical Studies of the Blood Serum and Treatment with Adrenocortical Extract, Dihydrochysterol or Vitamin D, *New England J Med* 231 44-51 (July 13) 1944.

8 Tomlinson, C. C., and Cameron, O. J. Juvenile Pemphigus. Effects of Germanin in Three Cases, *Arch Dermat & Syph* 38.555-568 (Oct) 1938.

9 Becker, F. T., in discussion on Michelson, H. E. Pemphigus Vulgaris Showing Remission After Treatment with Germanin, *Dermatitis Medicamentosa*, *Arch Dermat & Syph* 36:240 (July) 1937.

10 Wells, H. G., Humphreys, E. M., and Work, E. G. Significance of Increasing Frequency of Selective Cortical Necrosis of the Adrenal as Cause of Addison's Disease, *J A M A* 109 490-493 (Aug 14) 1937.

son's disease, except there was no evidence of regeneration. The entire cortical epithelium had almost disappeared leaving stroma containing only distended capillaries, round cells and occasional groups of living cortical cells which were abnormally large."

Balbi<sup>11</sup> found "a state of maceration and disorganization so that many areas could not have been secretory. Other areas show degenerative changes varying in extent and severity and small foci of infiltration. We are dealing with a real, acute interstitial suprarenitis of nodular variety." In a second case there were a patchy depletion of lipids and a scanty zona reticularis. In 2 there were only adenomatous changes, and in 1, "advanced putrefaction." Talbott and others<sup>3</sup> found occasional foci of lymphocytic infiltration especially in the region

in 1 case. Buschke and Langer<sup>15</sup> found "atrophy" in 1 case and Foldvari<sup>16</sup> "hypoplasia" and "atrophy" in 2. Gellis and Glass<sup>6</sup> found a thickened, nodular cortex in 1 case. Eliassow and Sternberg<sup>17</sup> found advanced tuberculosis of the adrenals in a single case of pemphigus.

#### REPORT OF CASES

**CASE 1**—The patient was a 76 year old white woman. The duration of the disease was thirty-two days.

She was hospitalized because of chronic heart failure. A mild itching of the back had been noted for two weeks. Twelve days after she was admitted to the hospital palmar erythema was noted, and examination of the back revealed many large bullae. Nikolsky's sign was elicited. The bullae spread rapidly, and the patient's temperature hovered about 101 F and rose terminally to 104.5 F.

**Autopsy**—The entire skin was covered with bullous lesions, many of which had rubbed off, and others

#### *Description of the Adrenal Glands in the Autopsy Protocols of 105 Cases of Pemphigus*

| Observer  | Cases Reported | Adrenals Not Mentioned | Adrenals "Normal" | "Post-mortem Autolysis" | Inadequate Description | Detailed Description |
|---|----------------|------------------------|-------------------|-------------------------|------------------------|----------------------|
| Talbott, Lever and Consolazio <sup>3</sup>                            | 7              | 1                      | 2                 |                         | 3                      | 1                    |
| Gellis and Glass <sup>6</sup>   | 9              |                        | 6                 | 2                       | 1                      |                      |
| Balbi <sup>11</sup>   | 5              |                        |                   |                         | 1                      | 4                    |
| Wells, Humphreys and Work <sup>10</sup>                               | 1              |                        |                   |                         |                        | 1                    |
| Buschke and Langer <sup>15</sup>                                      | 1              | -                      |                   |                         | 1                      |                      |
| Buschke, A., and Ollendorff, H. <i>Dermat Wchnschr</i> 81: 1591, 1925 | 1              | -                      |                   |                         | 1                      |                      |
| Chiari <sup>13</sup>  | 10             | 1                      | 2                 |                         | 7                      |                      |
| Eliassow and Sternberg <sup>17</sup>                                  | 1              |                        |                   |                         | 1                      |                      |
| Fivoli <sup>12</sup>  | 23             | 2                      |                   | 1                       | 19                     | 1                    |
| Foldvari <sup>16</sup>  | 37             | 35                     |                   |                         | 2                      |                      |
| Martinotti, L. <i>Gior ital di dermat e sif</i> 63: 504, 1928         | 5              |                        | 5                 |                         |                        |                      |
| Sarason <sup>14</sup>   | 1              |                        |                   |                         | 1                      |                      |
| Tobias, H. <i>Am J Dis Child</i> 48: 1064 (Nov) 1934                  | 1              | 1                      |                   |                         |                        |                      |
| Tomlinson and Cameron <sup>8</sup>                                    | 1              |                        |                   |                         |                        | 1                    |
| Werth, J. <i>Arch f Dermat u Syph</i> 183: 483, 1942                  | 2              | 2                      | -                 |                         |                        |                      |
| <b>Total</b>  | <b>105</b>     | <b>42</b>              | <b>15</b>         | <b>3</b>                | <b>37</b>              | <b>8</b>             |

of "small necrotic areas." In a second case there was infarction of the left adrenal, in a third there were "cystic changes of the medulla," and in a fourth bilateral hemorrhages and a necrotic medulla. In the last case the cortical cells were said to be "well preserved"—a conclusion which seems rather doubtful. Fivoli<sup>12</sup> found degeneration and loss of cortical cells in 1 case. Chiari<sup>13</sup> noted "initial degeneration," "initial fibrosis in the reticularis" in 7 cases, conditions dismissed as postmortem changes. Sarason<sup>14</sup> found what he classified as acute toxic changes

were covered by thick yellow crusts. Evidences of aortic stenosis, chronic cholecystitis and cholelithiasis, atrophic gastritis and early bronchopneumonia were found.

**Adrenals** Gross examination. The glands were somewhat grayish with yellow flecks. The area of the corticomedullary junction was soft and friable.

**Microscopic examination** There were small isolated islands of cortical cells clustered about the main artery some distance from the adrenal. A few ganglions and their nerve bundles were surrounded by a pronounced infiltration of lymphocytes and plasma cells. The capsules were normal. The zona glomerulosa had striking rectangular and wedge-shaped areas of necrosis (fig 1) surrounded by a zone of congestion, and only cellular outlines remained within these areas. Otherwise, the

11 Balbi, E. Pemfigo e ghiandole endocrine, *Arch ital di dermat, sif* 6: 103-141 (Nov) 1930.

12 Fivoli, C. Contributo allo studie anatomopatologico nel pemfigo, *Dermosifilograf* 11: 1-43 (Jan) 1936.

13 Chiari, G. Repertu istopatologici di ghiandole endocrine in dieci casi di pemfigo, *Gior ital di dermat e sif* 73: 116-124 (Feb) 1932.

14 Sarason, E. L. Adrenal Cortex in Systemic Disease, *Arch Int Med* 71: 702-712 (May) 1943.

15 Buschke, A., and Langer, E. Pemphigus und innere Sekretion, *Dermat Wchnschr* 38: 1571-1578 (Oct 23) 1926.

16 Foldvari, F. Der gegenwartige Stand der Pemphigus-frage, nebst pathologischen, experimentellen und therapeutischen Erfahrungen, *Acta dermat-venereol* 16: 233-261 (Oct) 1935.

17 Eliassow, A., and Sternberg, A. Ein Fall von Pemphigus foliaceus nebst Bemerkungen über die Todesursache bei Pemphigus, *Dermat Ztschr* 42: 186-196 (Nov) 1924.

zona glomerulosa was generally well preserved. Most of the cells were of average size, and the cytoplasm was granular and slightly basophilic. There were, however, numerous cells with scanty cytoplasm and pyknotic, intensely basophilic nuclei. Only finely granular lipid was present in the cells. There was uneven engorgement of the interglomerular capillaries. There was no stromal proliferation. Small patches of lymphocytes were visible. The zona fasciculata was disarranged by a number of small nodules whose cells were somewhat larger than those of the surrounding parenchyma. Many cords were broken by necrosis or complete disappearance of the cells, leaving collapsed, empty stroma

granule. In the medulla no changes were observed, except in the islands of cortical cells which were undergoing degeneration.

CASE 2—The patient was a 58 year old white woman. The duration of the disease was from ten to eleven weeks.

Eight to nine weeks before the patient was admitted to the hospital a "blood blister" appeared on the leg and gradually spread over the extremity, and finally blisters became generalized. The patient slowly became drowsy, irrational and incontinent. Physical examination revealed a bullous and pustular eruption and a moderately enlarged liver. The value for nonprotein

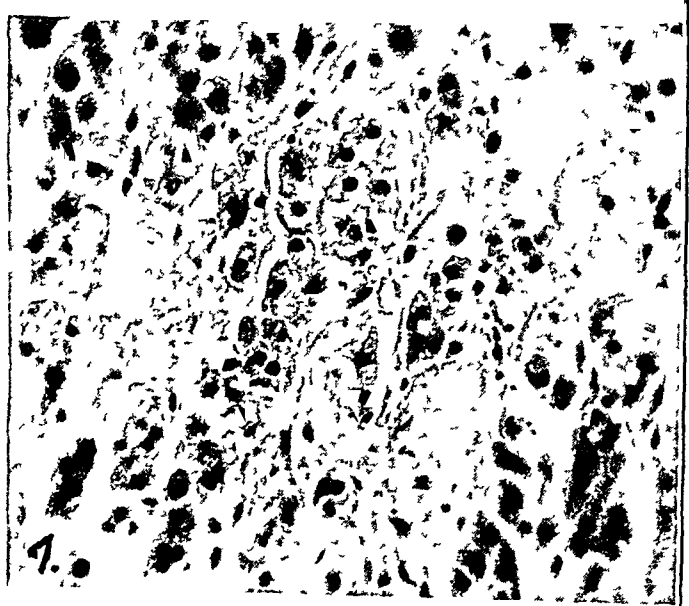
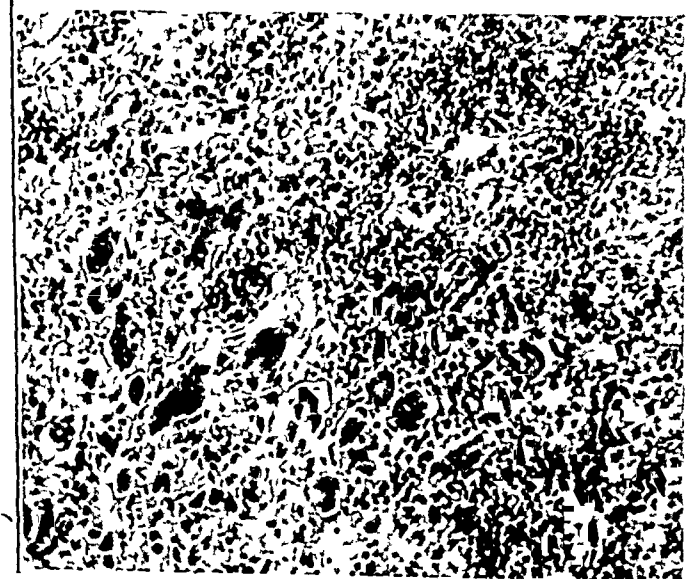
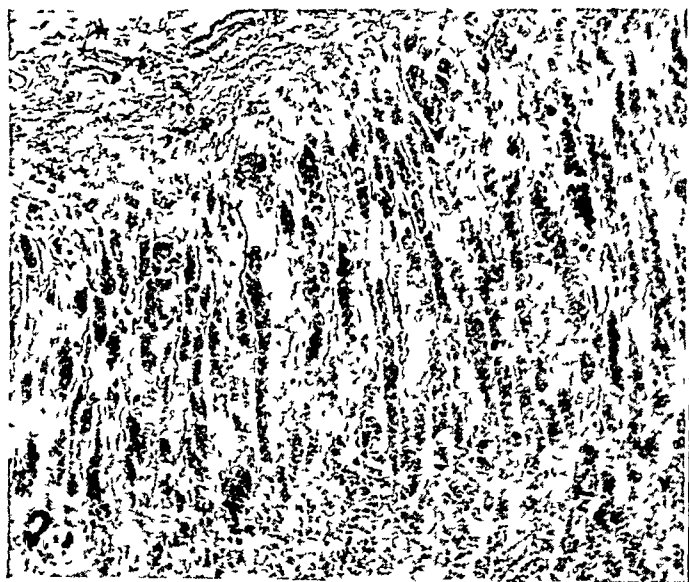
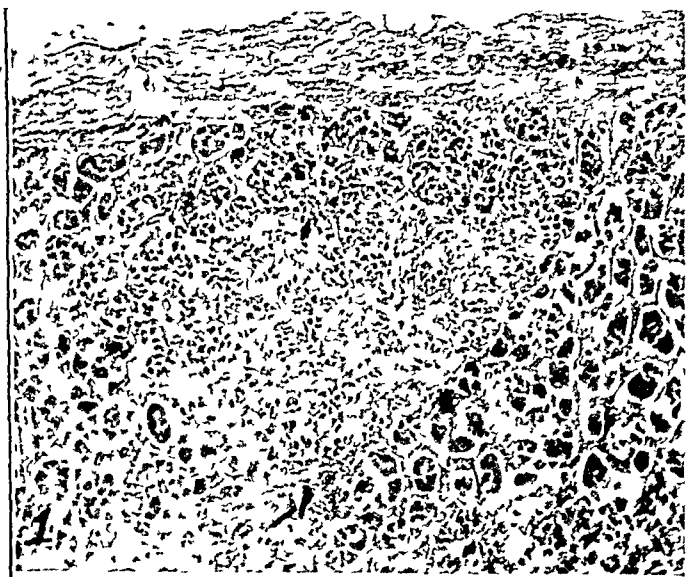


Fig 1 (case 1)—Wedge-shaped area of disrupted necrotic cortical cells surrounded by a zone of intense congestion (arrow). Mallory's acid fuchsin stain.

Fig 2 (case 6)—Loss of glomerular layer. Decided destruction of columns of the zona fasciculata. Hematoxylin and eosin stain.

Fig 3 (case 2)—Intense infiltration of the zona reticularis with lymphocytes and plasma cells. Marked loss of parenchyma. Hematoxylin and eosin stain.

Fig 4 (case 2)—Extensive destruction of the fasciculate layer. Note the absence of spongiocytes. Hematoxylin and eosin stain.

Occasionally only loosely scattered cells were left, even the best preserved of these were small and basophilic. The capillaries of the zona reticularis were engorged and the stroma was prominent, but there was no evidence of proliferation. There was decided fatty change. The scanty parenchyma consisted of small brown-pigmented cells with an occasional coarse lipid

nitrogen was 121 mg per hundred cubic centimeters, rising to 275 mg terminally. Albuminuria was constant. Low grade fever was present throughout the twelve day hospital course.

Autopsy—A generalized bullous, pustular and hemorrhagic eruption involved the skin, mucous membranes and conjunctivas. Evidences of pulmonary edema, early

bronchopneumonia, acute and chronic cystitis and chronic pyelonephritis were found

**Adrenals** Gross examination The color was grayish and the consistency firm No evidences of hemorrhages or cavitation were found

**Microscopic examination** (fig 5) Small foci of lymphocytes were observed in the pericapsular tissue One small ganglion and the radiating nerves were surrounded by a cuff of round cells The capsule was thin, the fibrils were hyalinized, and occasional fibroblasts were seen The zona glomerulosa had small groups of atrophic cortical cells scattered throughout the prominent stroma, but it was well preserved in other areas The zona fasciculata was irregularly narrowed, consisting of isolated cell groups separated by an ample stroma, in which degenerating cortical cells were still visible (fig 4) In other areas, there was irregular, nodular proliferation of cortical cells, which were mostly small and acidophilic No spongiocytes were found anywhere, but some of the cells contained scanty finely granular lipid The zona reticularis was rather broad, and its cells contained golden brown pigment or showed advanced stages of disintegration The capillaries were engorged, and a few small fissures were observed There was intense lymphocytic infiltration, which in one area almost replaced the parenchyma (fig 3) The medulla was interspersed with groups of acidophilic cortical cells, otherwise, it was entirely normal

**CASE 3**—The patient was an 81 year old Negro The duration of the disease was about four months

Three to four months before admission to the hospital the patient was struck by a wooden chip, and the area involved became infected Blisters formed around it and then spread, becoming generalized The patient suffered severe malaise, chills and progressive weakness Physical examination revealed signs of a recent loss of weight, a generalized eruption sparing only the face and palms, and a general lymphadenopathy Examination of the blood showed 27 mg of nonprotein nitrogen, 130 mg of sugar, 80 mg of cholesterol, 33 mg of cholesterol esters and 406 mg of chlorides per hundred cubic centimeters The course was steadily downhill, and death occurred on the sixteenth hospital day

**Autopsy**—A bullous, pustular and crusted eruption involved the skin, oral mucosa and conjunctivas There was a sacral decubitus ulcer Evidences of acute bronchopneumonia, chronic cystitis, prostatic hypertrophy and a carcinoid of the ileum were found

**Adrenal** Gross examination In one gland there was a grape-sized nodule of a bright yellow color in contrast to the rest of the tissue, which had a darker grayish hue No traces of hemorrhages or cavitation were observed

**Microscopic examination** There was considerable fibrosis of the pericapsular tissue The arteries showed atheromatous plaques No ganglions were found, the nerves showed no round cell cuffing There was hyalinization of the capsular collagenous fibrils, and lymphocytes infiltrated the subcapsular zone The cortex and medulla showed an irregular line of junction The large adenoma was entirely within the gland, and a sharp border between cortex and adenoma was formed by compressed, acidophilic cells and delicate fibrous stroma The zona glomerulosa was irregular and narrow and in some areas entirely absent The cells were small with wrinkled nuclei Thickened radial septums traversed the cortex The zona fasciculata was barely recognizable, only a few atrophic trabeculae were left

and the site of others was indicated by empty columns and fragments of cells Nodules formed by large acidophilic cells produced further distortion (fig 7) The cells showed all stages of disintegration, an occasional spongiocyte could be seen, but there were few lipid granules in even the best preserved cells The zona reticularis consisted of fairly large cells with granular and at times vacuolated cytoplasm and many brown pigment granules Many degenerating cells were seen, and round cells were scattered throughout In the capillaries there was patchy engorgement The adenoma consisted mainly of large foamy cells, whose contents stained pink with Nile blue sulfate The architecture seemed chiefly trabecular, with more medullary areas formed by densely packed acidophilic cells showing scanty lipids in a fine granular dispersion The medulla was represented by a few nests of pheochromic cells, which were large and stained well Cortical nodules clustered about the central vein, which showed decided muscular hypertrophy

**CASE 4**—The patient was a 61 year old white woman The duration of the disease was about four and a half months

Nine weeks before being admitted to the hospital, this woman with hypertension and diabetes had a vesicular and bullous eruption, which healed and recurred One week before she was admitted, oral lesions developed There were noticeable malaise and progressive weakness Physical examination revealed a generalized bullous eruption The blood pressure was 180 systolic and 100 diastolic Examination of the blood showed sugar, 250 to 93 mg, nonprotein nitrogen, 27 mg, urea nitrogen, 11 mg, and cholesterol, 390 mg per hundred cubic centimeters The diabetes was controlled The temperature was irregular and rose gradually Death occurred on the seventy-second hospital day

**Autopsy**—A generalized eruption involved the skin and the oral and vulvar mucosa There was a sacral decubitus ulcer Evidences of early bronchopneumonia, cloudy swelling of the liver and kidneys, acute splenic hyperplasia and fibromyomas of the uterus were found

**Adrenals** Gross examination There was decided irregularity in thickness The tissue was friable, but no traces of hemorrhages or cavitation were found

**Microscopic examination** A small sympathetic ganglion showed no changes, but eccentric patches of lymphocytes were found along emergent nerve bundles There were many extracapsular nodules of cortical cells, which at times extended loosely into the surrounding areolar tissue There were atherosclerosis and calcification of the peripheral arteries The capsule was irregularly thickened, and nests of cortical cells, lymphocytes and fibroblasts were found in the thickened areas The zona glomerulosa showed decided interstitial fibrosis The cells were very small The zona fasciculata varied in width and architecture Nodular hyperplasia was greatly in evidence Occasional trabeculae were intact, and others were disintegrated and showed advanced necrosis of the parenchyma The intact cells were small and uniformly depleted of lipids, and no spongiocytes were found The zona reticularis was entirely absent in spots Numerous fissures were seen The parenchymal cells were small and necrotic Bacterial emboli were common, and patches of lymphocytes were found The medulla was patchy and interspersed with cortical tissue

**CASE 5**—The patient was a 60 year old white man The duration of the disease was about six months



About five months before he was admitted to the hospital, a "pimple" appeared on the nose and grew rapidly. Other lesions appeared and spread rapidly, becoming generalized. There was decided malaise, severe itching at times and a disagreeable odor. Physical examination showed otherwise normal conditions. The course was steadily downhill and the patient died on the twenty-fifth hospital day.

*Autopsy*—The skin was covered with bullae up to 4 inches (10 cm) in diameter, some with fleshy, shiny bases and others with black crusts. Evidences of minimal bronchopneumonia, toxic myocarditis, prostatic hypertrophy, perisplenitis and esophageal varices were found

hyaline. The zona glomerulosa was broad with the stroma greatly increased. The cells appeared small and depleted of lipid, though occasional spongiocytes were seen. In the zona fasciculata a few columns were still intact, many had disappeared entirely, leaving empty spaces, or had disintegrated into individual decaying cells. Nodular hyperplasia formed groups of intensely staining cells. Occasional lymphocytic foci were seen. The zona reticularis was destroyed in most places by cavitation and fissuring, but a few of the intact cells contained large lipid droplets and the capillaries were intensely engorged. The medulla showed no changes. A large ganglion within the

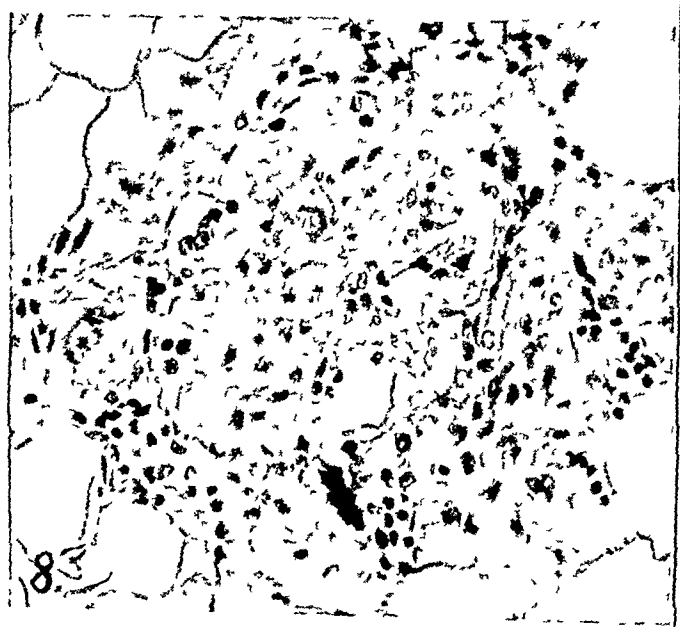
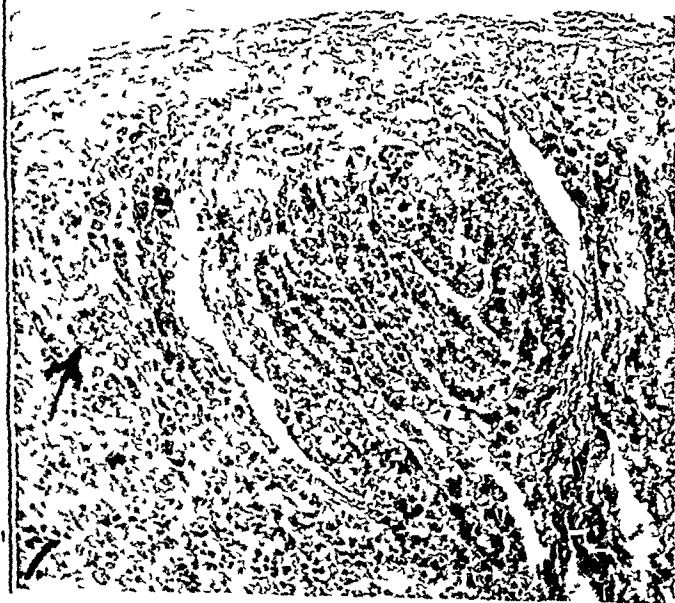
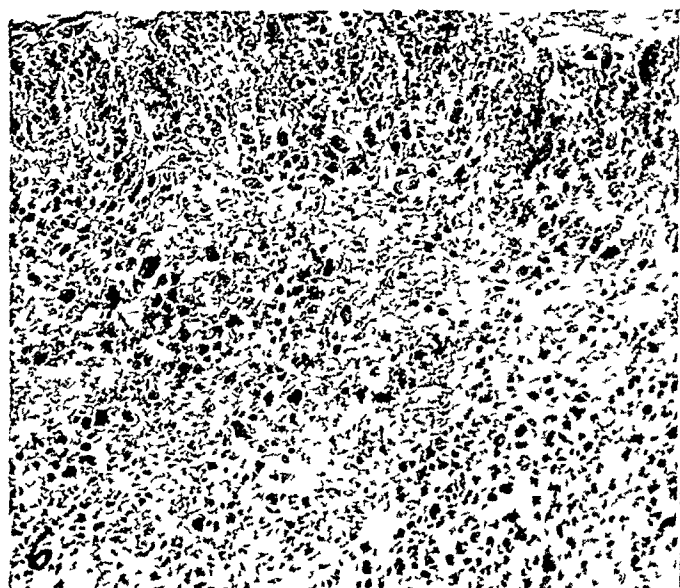
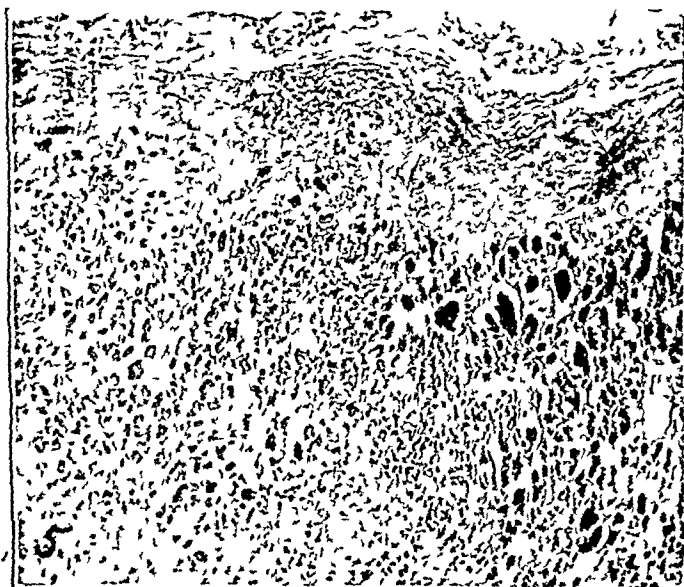


Fig 5 (case 2)—Complete destruction of the cortical architecture with beginning fibrosis of the capsule and the glomerular layer. Mallory's acid fuchsin stain.

Fig 6 (case 5)—Complete rebuilding of the cortex, with extensive cell loss and cirrhosis. Mallory's acid fuchsin stain.

Fig 7 (case 3)—Large hyperplastic nodule, showing the same degenerative changes as the surrounding parenchyma. The arrow indicates a clump of round cells. Hematoxylin and eosin stain.

Fig 8 (case 5)—Small sympathetic ganglion surrounded by lymphocytes and plasma cells. Hematoxylin and eosin stain.

*Adrenals* Gross examination. Advanced cavitation was found, but there was no sign of hemorrhage. The color was a homogeneous buff throughout.

Microscopic examination (fig 6). There were many extracapsular cortical nodules. A small sympathetic ganglion was surrounded by round cells (fig 8). The capsule was thick and the collagenous fibers densely

medulla showed degenerative changes of the ganglion cells.

**CASE 6**—The patient was a 50 year old Negro woman. The duration of the illness was about eight months.

Seven months before the patient was admitted to the hospital, a generalized bullous eruption developed. On admission she also had a purulent conjunctivitis.

Laboratory examination revealed slight albuminuria, a positive reaction (4 plus) to the Wassermann test, a nonprotein nitrogen content of 22 to 27 mg and a blood sugar level of 87 to 105 mg per hundred cubic centimeters. The course was progressively downhill, with a constant, low grade fever rising terminally to 103 F.

**Autopsy**—Generalized bullae alternated with areas of denudation and black hyperkeratotic skin. Evidences of bilateral bronchopneumonia, thrombosis of the cavernous sinus and left iliac, renal, ovarian and adrenal veins and fibromyomas of the uterus were found.

**Adrenals** Gross examination An anomalous left adrenal vein which was occluded by a friable thrombus was observed. The right adrenal was grayish, and the left was a brighter yellow. There were no hemorrhages or cavitation.

**Microscopic examination** The peripheral vessels of the left adrenal were engorged, and one capillary showed a bacterial embolus. Many extracapsular nodules of cortical tissue were seen, some proliferating loosely into the adjacent areolar tissue. Ganglions and nerve bundles were surrounded by patches of round cells. The capsule showed irregular thickening and increased collagen, while the tissue of the left adrenal showed beginning infarction. The zona glomerulosa was narrow, with the cells being small and depleted of lipid. The stroma was decidedly increased. The zona fasciculata was distorted by nodules of cortical cells and by the disappearance of single cells or entire columns (fig 2). The remaining cells were small and basophilic, and occasional cells within the nodules contained lipids. The cells of the left adrenal were somewhat larger, and occasional spongiocytes could be seen. The zona reticularis where present consisted of disintegrating cells bearing pigment granules. There was considerable capillary engorgement in the left adrenal. The medulla showed no architectural changes. Small organized thrombi, occasionally calcified, were seen bilaterally.

#### COMMENT

It is at once apparent that in all 6 cases extensive and decidedly similar changes were manifest. These may be grouped as follows: acute degenerative and inflammatory changes, necrobiosis and loss of cells, depletion of lipid, nodular hyperplasia and fibrosis. They demonstrate a definite pattern of development. Thus the wedge-shaped areas of necrosis seen in case 1 and the intense round cell infiltration of case 2, coupled with the minimal nodular hyperplasia in both cases and the beginnings of fibrosis in case 2, are fully consistent with the relatively short duration of the disease. Cases 3 to 6 indicate that the longer the course of the disease the more pronounced are the fibrosis and nodular regeneration. These changes are evidences of continued damage to the adrenals leading to scarring and attempts at regeneration, which finally produce a pattern comparable to the changes of hepatic architecture in Laennec's cirrhosis. However, there was more hyperplasia in case 5 than in case 6, but an absolutely rigid parallelism with the duration of the disease is hardly to be

expected. Generalized depletion of lipid, diminution of the size of the cells and diffuse degenerative changes of the parenchyma were found in all 6 cases, and they imply important functional changes.

In addition, the round cell infiltration about the small sympathetic ganglions and nerves is of interest. This infiltration was in evidence in 4 cases, in a fifth case only a few nerve bundles showed the change, and in the sixth no ganglions could be found but the nerves showed no infiltration. It is true that small foci of round cells are to be found within almost any adrenal and can hardly be considered abnormal, but infiltration of the nerve elements seems unquestionably pathologic. At the present time, any explanation of this fact would be purely speculative. Other changes, such as degeneration of the medullary ganglion cells in case 5 and old thrombi and fresh thrombosis and infarction in case 6, are to be considered as incidental. The presence of bacterial emboli in 2 cases is apparently terminal in view of the absence of inflammatory reaction, and does not explain changes which were also present in areas where no bacteria were found.

Although the lesions in all 6 cases were strikingly similar, there is nothing to indicate that they were either specific or pathognomonic. Lucien and Parisot<sup>18</sup> illustrated histologically almost identical tissue, presumably not from a person with pemphigus, in their description of the sclerosing, atrophic process which occurs in the adrenals during chronic infectious diseases of all sorts. They stated that they had seen essentially similar changes in tuberculosis, but during my experience I have not seen such changes. Garb<sup>19</sup> found biochemical evidence of adrenal cortex insufficiency in a case of bullous mycosis fungoides. In a single case (nonbullous) which I have observed at autopsy no degenerative changes or depletion of lipid was found.

It must be pointed out that the lesions found in this series could not be due to any concomitant infection which existed at the time of death. It is true that loss of lipids, fissuring and cavitation, as well as lymphocytic infiltration, are commonly seen in persons with acute infectious diseases, particularly bronchopneumonia.<sup>20</sup> However, hemorrhages into the cortex or the changes re-

18 Lucien, M., and Parisot, J. *Les glandes surrénales et organes chromaffines*, Paris, 1913, p. 289, fig. 74.

19 Garb, J. *Mycosis Fungoides with Bullous Lesions*. Special Tests and Laboratory Data Indicating Adrenal Insufficiency, *Arch. Dermat. & Syph.* **49**: 315-320 (May) 1944.

20 Oppenheim, R., and Loeper, M. *L'insuffisance surrénale expérimentale par lésions des capsules*, *Compt. rend. Soc. de biol.* **55**: 330-332, 1903.

ately described by Rich<sup>21</sup> as characteristic of acute infections are conspicuously absent in all my cases. Moreover, the occurrence of wedge-shaped necrosis does not belong to the picture of ordinary infection, nor does the diffuse disintegration of the zona fasciculata or the extensive loss of architecture.

In view of these observations it is hardly surprising to note the development of Addison's disease after pemphigus, especially when the regenerative ability of the adrenals seems to have been defective. Balbr's "nodular, interstitial supranephritis"<sup>11</sup> is apparently identical with the picture I have observed. The frequently noted, less definite findings of "small necrotic areas,"<sup>3</sup> "atrophy," "hypoplasia,"<sup>16</sup> "nodular hyperplasia"<sup>6</sup> and "postmortem autolysis" become highly suggestive, and the "initial fibrosis of the reticularis" of Chiale,<sup>13</sup> which he apparently erroneously interpreted as a postmortem change, seems simply a less advanced stage of the process seen in figure 6. Thus one seems justified in assuming that careful histologic examination of the adrenals in persons with pemphigus will yield positive, significant findings far more consistently than the literature seems to indicate.

A cortex deprived of its lipid load and showing cell necrosis and deranged architecture is hardly capable of adequate secretory function. This does not necessarily mean that production of hormones has ceased altogether but merely that there are quantitative and perhaps qualitative changes.

Certain correlations can be drawn between the evidence of impairment of the adrenal glands and the clinical picture of pemphigus. It is known that in adrenal cortical insufficiency there is a decreased resistance to infection.<sup>22</sup> There is also an increased permeability of the capillaries, as a result of which plasma escapes from the blood stream.<sup>23</sup> This fluid is usually taken up into the intracellular compartment with no trend to edema, but with local changes in the skin it may

possibly contribute to the formation of vesicles and Nikolsky's sign.

The biochemical changes in patients with pemphigus are not unequivocal. The decrease in urinary excretion of chlorides first noted by Krieger<sup>1</sup> has been corroborated by other investigators.<sup>24</sup> The serum chloride, as determined by various investigators,<sup>25</sup> was found to be high, low or normal. These discrepancies apparently represent different stages or degrees of adrenal involvement. At any rate, the findings of Talbott and others<sup>3</sup> show that in exacerbations of acute pemphigus the electrolyte pattern of the blood is almost identical with that in an Addisonian crisis. An increase of nonprotein nitrogen and plasma potassium is accompanied by a corresponding fall in sodium and chloride. It is remarkable that these studies revealed increased volumes of blood, plasma and interstitial fluid in patients with both acute and chronic pemphigus as long as cutaneous lesions were present. These observations, which do not fit into the present concept of adrenal insufficiency, cannot be explained adequately and may be due to other factors unrelated to the adrenal lesions.

It must be emphasized that pemphigus is by no means a primary adrenal disease, on the contrary, the causative agent of pemphigus produces damage to the adrenals as a complication of the cutaneous disease. This complication, however, as in many other diseases, may contribute greatly to the symptomatology, course and eventual outcome of the disease.

#### SUMMARY AND CONCLUSIONS

The changes in the adrenals in 6 cases of pemphigus are described.

Regressive changes were present in all cases, and the extent of interstitial changes was commensurate with the duration of the disease.

The changes described are compatible with the view that the function of the adrenal is impaired in persons with pemphigus.

21 Rich, A. R. Peculiar Type of Adrenal Cortical Damage Associated with Acute Infections and Its Possible Relation to Circulatory Collapse, *Bull. Johns Hopkins Hosp.* **74** 1-15 (Jan.) 1944.

22 Pottenger, F. M. Neural and Endocrine Factors in Bodily Defense, *Endocrinology* **21** 449-454 (July) 1937.

23 Menkin, V. Effect of Adrenal Cortex Extract on Capillary Permeability, *Am. J. Physiol.* **129** 691-697 (June) 1940.

24 Zorn, R., and Popchristoff, P. L'élimination urinaire des chlorures dans les affections bulleuses et vésiculeuses de la peau, *Ann. de dermat. et syph.* **5** 667-696 (July) 1934. Cassaet and Michelet.<sup>2</sup>

25 Urbach, E. Zur Pathochemie des Pemphigus, *Arch. f. Dermat. u. Syph.* **150** 52-70, 1926. Kartamischew, A. Ueber die Oedembereitschaft bei Pemphigus vegetans, *ibid.* **143** 184-192, 1923. Berhardt, R. Weitere Beiträge zur Ätiologie des Pemphigus und der Duhringschen Krankheit, *ibid.* **171** 536-555, 1934. Talbott, Lever and Consolazio.<sup>3</sup>

# CUTANEOUS AND SUBCUTANEOUS LESIONS OF THE LOWER LIMBS IN CONNECTION WITH THE VEINS

## DIFFERENTIAL DIAGNOSIS

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In a great many dermatoses the limitation of eruptions to certain areas is often dependent on the distribution of the blood vessels in these regions. The relationship manifests itself either in an increased susceptibility to localized outbreaks or, more rarely, in a tendency to suppression.<sup>1</sup> This observation can be substantiated by demonstration of cutaneous lesions in close proximity to superficial visible veins (fig 1) or to subcutaneous palpable veins. Infra-red photography<sup>2</sup> or phlebography<sup>3</sup> reveals the relationship between cutaneous lesions and concealed venous channels. The topographic coincidence may be visualized on any part of the body, but it is more apparent in areas with prevalent vascular disturbances, as, for example, on the lower extremities where, owing to generally unfavorable mechanical conditions, congestion easily develops. Hemostasis, even of slight degree, favors the appearance of cutaneous eruptions on the legs. The aggravation of symptoms corresponds to the progressive impairment of the venous circulation.

Severe and permanent changes are to be expected as a consequence of long-standing varicose veins. Chronic stagnation not only interferes with the adequate nutrition of the affected areas but also increases the tendency to recurrent phlebitis and inflammatory reactions in the perivenous tissues. The surface of an entire limb may become modified by ensuing atrophic or, more frequently, hypertrophic changes. Cutaneous lesions accompanying the "varicose symptom complex" may deviate from their usual clinical aspect, and difficulties may be encountered in their interpretation.

The recognition of the etiologic role of the veins in the development of all cutaneous manifestations of the limbs is important not only from the diagnostic but also from the therapeutic standpoint.

The early treatment of the deficient circulation may prevent further complications and save the patient much discomfort in the future.



Fig 1—Scleroderma en bandes along varicose veins

SYMPTOMS AND SIGNS OF BEGINNING HEMOSTASIS

One of the first signs of venous stasis, of increased capillary pressure and of capillary per-

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1 Abramowitz, E W, and Isaak, L. Lichenoid Amyloidosis. Report of Two Cases Featuring Absence of Cutaneous Lesions Over Some of the Tributaries of the Internal Saphenous Veins, *Arch Dermat & Syph* 40 13 (July) 1939

2 Zimmerman, L M, and Rattner, H. Infra-Red Photography of Subcutaneous Veins, *Am J Surg* 27 502 (March) 1935. Hathausen, H. Infra-Red Photography of Subcutaneous Veins, *Brit J Dermat* 45 506 (Dec.) 1933

3 Wolf, M, and Remenovskiy, F. Die praktische Anwendung der Varicographie, *Wien klin Wchnschr* 44 353 (March 13) 1931

meability may be edema of the dependent parts of the leg concomitant with pruritus. Itching is localized chiefly around the ankles, on the inside of the legs or on the shins. It increases toward evening after a day's work in an occupation that requires prolonged standing. Tiny papules are scattered among reddish discolored areas of the lower extremities, some of the lesions are covered with blood-stained brownish crusts, frequent scratching facilitates the gradual transition to eczematization.

Other cutaneous disorders may simulate these early stages of inadequate function of the veins. Lichen planus limited to the legs must be considered, but typical lichen planus lesions appearing later on the cheeks or in the genital regions or histologic examination which discloses the well known features of lichen planus will help to confirm the diagnosis.

Scratch marks confined to the legs may occur in persons with diabetes and may occasionally be mistaken for symptoms of hemostasis. Examination of the urine, determination of the blood sugar level or a high glucose tolerance curve will determine the true nature of the intense pruritus.

Some phases of blood dyscrasias manifesting themselves as prurigo on the lower limbs may be difficult to differentiate from hemostatic disturbances. Tiny itchy papules spread over a diffuse scaly dermatitis will not reveal the characteristics of leukemia, but repeated blood counts showing an increase of lymphocytes and a histologic picture of an enlarged lymph node will afford sufficient evidence for a diagnosis of prurigo lymphatica.

Another misleading sign in association with stasis is the occurrence of intracutaneous petechiae and pigmentations. Pinpoint-sized to pinhead-sized reddish spots changing to greenish brown and finally to dark brown usually form discrete nummular patches on all parts of the leg but mostly on the lower third. These ill defined lesions have a superficial resemblance in distribution and appearance to Schamberg's progressive pigmentary dermatosis and to the pigmented purpuric lichenoid dermatitis of Blum and Gougerot. But in Schamberg's disease,<sup>4</sup> observed more often among men, one finds first the same reddish puncta which by extending in size and by uniting with other lesions, develop slowly into irregularly contoured reddish brown eruptions. The patches may be marked by exag-

gerated skin lines and by satellite lesions, so-called cayenne pepper spots at the outer borders. The puncta gradually disappear, leaving a brownish discoloration. However, real petechiae are always missing. Furthermore, the absence of subjective sensations and of any form of dermatitis in the affected areas of the leg and, finally, the microscopic picture will support the diagnosis of Schamberg's disease. And in persons with pigmented purpuric lichenoid dermatitis<sup>5</sup> the lesions are pinhead-sized, elevated and papular, with the formation of flat, generally dark red plaques resembling lichen planus plaques. The individual papules do not enlarge peripherally and are discrete and regular, they later become purpuric and pigmented. Although the morphologic and clinical features of the aforementioned diseases are fairly distinctive and the histologic picture is well defined, some dermatologists believe that Schamberg's disease and pigmented purpuric lichenoid dermatitis are merely odd forms of stasis dermatitis.<sup>6</sup> The coexistence of superficial intracutaneous venules or telangiectases and the finding of deeper-seated varicosities by palpation will be additional criteria in favor of dermatitis hemostatica.

Purpura (Majocchi)<sup>7</sup> and angioma serpiginosum<sup>8</sup> may have a remote resemblance to gravitational dermatitis.

All these purpura-like diseases of the lower limbs are favorite topics of discussion among dermatologists, and the issues are not definitely settled. For instance, Goeckerman<sup>9</sup> has stated the belief that "Schamberg's disease, angioma serpiginosum and purpura annularis telangiectodes (Majocchi's disease) represent merely a terminology covering certain reasonably definite morphologic cutaneous pictures. They represent varying degrees of injury resulting from an internal toxin with predilection for the capillaries."

5 Wise, F, and Wolf, J. Pigmented Purpuric Lichenoid Dermatitis, *Arch Dermat & Syph* **31**:445 (April) 1935.

6 Laymon, C W, in discussion on Rattner, H, and Falk, A. Pigmented Purpuric Lichenoid Dermatitis of Gougerot and Blum, *Arch Dermat & Syph* **47**:455 (March) 1943. Ayres, S, Jr, and Anderson, N P. Purpuric Lichenoid Dermatitis of Gougerot and Blum, *ibid* **37**:1062 (June) 1938.

7 McKee, G M. Purpura Annularis Telangiectodes, *J Cutan Dis* **33**:129, 186 and 280, 1915.

8 Wise, F. Angioma Serpiginosum, *J Cutan Dis* **31**:725, 1913.

9 Goeckerman, W, in discussion on Ayres, S, Jr. Case for Diagnosis (Schamberg's Progressive Pigmentary Dermatitis?) *Arch Dermat & Syph* **44**:927 (Nov) 1941.

4 Templeton, H J. Progressive Pigmentary Dermatitis (Schamberg), *Arch Dermat & Syph* **16**:141 (Aug) 1927.

# VARICOSE SYMPTOM COMPLEX AND SEQUELAE<sup>10</sup>

Valvular insufficiency tends to increase the reverse blood flow and the hydrostatic back pressure. Varicose degeneration and dilatation of the veins extend to the smallest superficial branches, and the resistance of the tissues to trauma and infection becomes lowered by the consequent chronic edema. Eczematous conditions and ulcer formation are the outstanding features of the varicose state, phlebitis and periphlebitis may precipitate their development. The different stages of varicose eczema are characterized by branny scaling, or flakelike exfoliation alternating with moisture and crust formation. Bacteria and fungi find an excellent medium for propagation in the permanently engorged legs. Dermatophytosis between the toes or of the nails serves as a source of repeated reinfection of the limbs. Secondary infections by streptococci in the form of lymphangitis or attacks of recurrent erysipelas may be followed by enormous swelling of the legs. Even without these infections the chronic inflammation of the superficial layers of the skin may slowly spread to deeper parts of the cutis and to the subcutis and may produce hyperplastic tissue changes. The state of pseudo-elephantiasis may be accompanied with verrucous or papillary projections of skin.

Generalized cutaneous allergic reactions are often encountered as a consequence of chronic varicose eczema or varicose ulcers. The clinical picture may be confused by concurrent fungous infections of the feet, by sensitization to topical medicaments, such as sulfathiazole, or by any type of contact dermatitis. The detection of the responsible allergen and its elimination may be of great assistance in the improvement of generalized dermatitis in connection with varicose veins, although the final cure in some cases may be effected only after treatment of the degenerated veins.

## IMPAIRED VENOUS CIRCULATION AS A CAUSATIVE FACTOR OF NEURODERMATITIS OF THE LEGS

Patients susceptible to atopic eczema may demonstrate the topographic coincidence of neurodermatitis with varicosities. The usual type of neurodermatitis, which is characterized by leathery exfoliating patches, may be found on the inside of the knee joint surrounding the dilated greater saphenous vein or along the course of

degenerated tributaries. In some cases the veins may be detected better by palpation than by inspection<sup>11</sup>. In its early stage neurodermatitis of the limbs may be cured by elimination of incompetent feeding veins.

Lichen chronicus simplex (Vidal) may also exhibit the close connection with varicose veins. Frequent vigorous rubbing of the congested areas of the limbs causes flat polygonal shiny lichenoid papules or hard spherical nodular elevations which may be aggregated into extensive patches above the inner aspect or around the outer aspect of the ankle corresponding to the origin of the saphena magna or the saphena parva vein.



Fig 2—Neurodermatitis associated with an incompetent lesser saphenous vein

(fig 2) Lichen chronicus simplex should be distinguished from localized primary amyloidosis and from lichen planus verrucosus.

Prurigo nodularis, a severer variant of neurodermatitis, may develop as a final result of intense scratching caused by hemostasis. Hypertrophic, hard, extremely itchy, tumor-like nodules with a verrucous surface are found close to varicose veins on a generally lichenified base (fig 3). With the treatment of surrounding

10 Nobl, G. Der varicose Symptomenkomplex, seine Grundlage und Behandlung, Berlin, Urban & Schwarzenberg, 1918.

11 Heyerdale, W., and Cannon, E. E. Neurodermatitis Associated with Incompetent Greater Saphenous Veins, Arch Dermat & Syph 44 52 (July) 1941.



varicosities these nodules may occasionally diminish in size or may even disappear

#### VARICOSE THROMBOPHLEBITIS

One of the most frequent complications of varicosities is superficial thrombosis or thrombo-



Fig 3—Prurigo nodularis lesions close to varicose veins

phlebitis promoted by the prevailing degenerative changes of the venous inner lining and by retardation of the blood stream (Superficial varicose thrombophlebitis must be differentiated from thromboangitis obliterans and from the migrating type of infectious thrombophlebitis) Circulating bacteria in the anoxic and congested veins may precipitate the development of varicose thrombophlebitis Slight injury is not a causative factor but may be an exciting agent in inducing the outbreak of the dormant inflammation The thrombophlebitic process manifests itself along very small veins as a circular patch but more often along the larger veins as a superficial indurated tender cord with redness of the overlying skin If aneurysmal pouches of the wall of the vein are involved, dark bluish plum-sized prominent elevations may result

Varicose thrombophlebitis can be regarded as a natural healing process leading finally to obliteration of degenerated and useless blood vessels Induration, atrophy and pigmentation of the tissues about the veins are common sequelae of the phlebitic process The thrombotic veins at times become impregnated with calcium deposits so that hard formations, so-called phlebolites, are felt along the sclerosed varicosities Recanalization may occur, reestablishing the former state of elongation and tortuosity Repeated phlebitis of superficial varicosities may be followed by rarefaction of the wall of the vein and formation of linear channels covered by whitish atrophic skin with hyperpigmentation at the borders The veins and surrounding tissues in patients with secondarily infected varicose thrombophlebitis are apt to break down and form

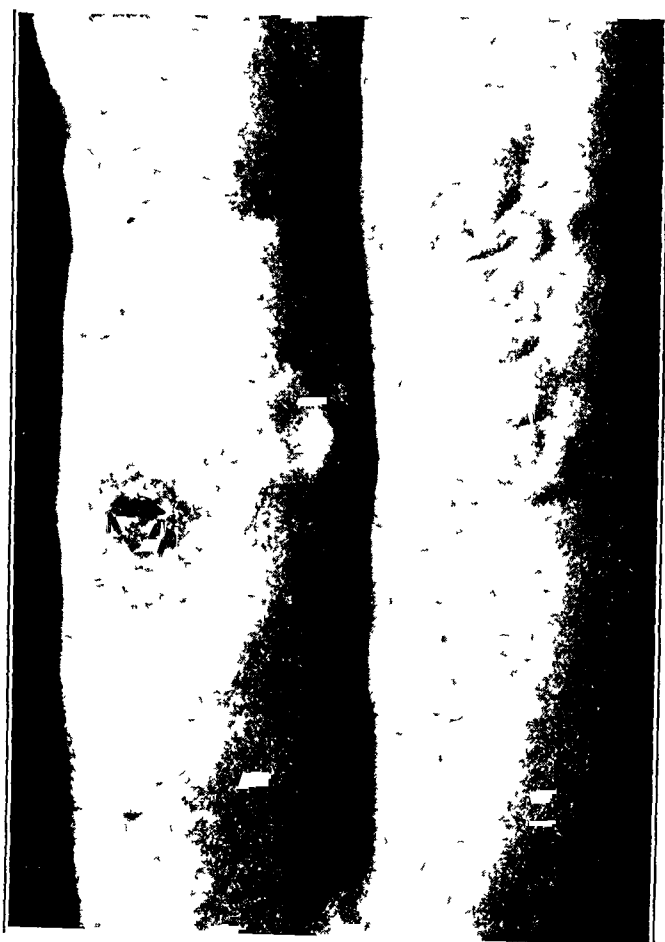


Fig 4—Thrombophlebitic ulcer resembling exulcerated erythema induratum

punched-out ulcers resembling ulcerated erythema induratum (Bazin) or syphilitic ulcers (fig 4)

#### DEEP PHLEBITIS AND SEQUELAE

Postoperative or puerperal phlebitis is entirely different from superficial varicose thrombophlebitis It is essentially, though not exclusively, limited to the deep veins Severe pain, fever, rigor and swelling of the entire leg are outstanding symptoms This type of phlebitis is



also called milk leg or phlegmasia alba dolens. Residual edematous changes and the appearance of superficial compensatory varicosities may depend on the degree of recanalization of the deep veins. Phlebography offers a reliable diagnostic criterion to determine with certainty the patency of the deep venous circulation after phlebotic processes.

The former shape of the affected limbs may occasionally be restored after subsidence of the acute symptoms. However, the permanent diffuse brownish purple discoloration and the tendency to repeated attacks of cellulitis are con-

deeper-seated varicosities. The inflammation becomes visible by the establishment of a brownish, indurated, palm-sized plaque on the leg above the inner side of the ankle, which may last indefinitely, with gradually increasing tenseness. The area may change its color to dark brown, it may become depressed below the surrounding surface by fixation to the subjacent tissues, and the inflammation may advance to the anterior and lateral aspect or may even continue to the upper third of the leg. Cufflike constrictions of sclerotic skin are characteristic features of this disease. Periostitic thickenings



Fig 5—A, ulcerated dermatosclerosis resembling idiopathic scleroderma, B, ulcerated idiopathic scleroderma with lilac-colored ring at the borders

firmatory evidence of the irreparable damage to the return circulation of the veins and lymph channels. The waterlogged tissues may gradually become atrophic and fibrotic. Ulcers in these undernourished parts of the leg may be called real phlebotic ulcers, which resemble ulcers occurring in dermatosclerosis.

#### PERIVENOUS PACHYDERMA OR DERMATOSCLEROSIS

Perivenous pachyderma or dermatosclerosis is a special type of inflammatory process which starts insidiously in the periphery of smaller,

similar to those in tertiary syphilis may be perceptible.

This chronic progressive induration, which almost always is associated with varicose veins, is called by German authors "dermatosclerosis," and by French authors pachydermie, it was described by G. Nobl<sup>12</sup> under the name of *perivenose Pachydermie*. Gaugier<sup>13</sup> explained it

12 Nobl, G. Das verkannte Zustandsbild der perivenösen Pachydermie, *Med Klin* 31: 580 (May 3) 1935.

13 Gaugier, L. Pathologie de l'appareil circulatoire (cœur et vaisseaux), in Rogen, G. H., Widal, F., and Teissier, P. J. *Nouveau traité de médecine*, Paris, Masson & Cie, 1933, vol 3, pt 10, pp 577-593 and 665-714.

as a microbic infection of the connective tissue without involvement of the veins and called it "cellulite" Biegeleisen,<sup>14</sup> who termed it "fibrolymphedema," assumed that the phlebotic infection extends to the perivenous tissues and involves the lymph channels and that complete blockage of the thrombosed lymph vessels causes chronic lymphedema, consequent hypertrophy of the connective tissue and finally fibrosis.

The sclerotic atrophic tissues are liable to break down and form chronic ulcers. If dilated or hardened veins are found in or above the involved areas the whole picture is easily understood, but diagnostic difficulties may arise if superficial varicosities are missing. The resemblance to localized scleroderma is occasionally striking, especially if the indurated parts become depigmented (fig 5 A). Localized scleroderma, however, is more ivory colored, and the borders are usually sharp and round and are often surrounded by a lilac-colored ring (fig 5 B). Typical morphea patches may be seen on other parts of the body, whereas fibrolymphedema is present only on the lower limbs and is poorly demarcated.

#### PHLEBITIS-LIKE NODULAR LESIONS OF THE LOWER LIMBS

It is a well known fact that the same cutaneous reaction may be produced by a number of agents, this holds true for nodular and ulcerating lesions around the veins of the leg. The causative factors may be various bacterial embolic processes or toxic and chemical influences. The lesions are mainly inflammatory reactions about the thrombotic veins, but in different phases the nodules may assume the clinical aspect of varicose thrombophlebitis involving the smaller veins and subsequent ulcerations may simulate varicose ulcers.

Erythema induratum (Bazin) usually starts on the posterior surface of the lower limb at the transition to the middle third, but lesions are also found on the lateral and outer aspects of the legs and more rarely, on the thighs and arms. Globular, hard cutaneous-subcutaneous nodules, the size of a hazelnut, are discernible by palpation. The confluence of single nodules may lead to the development of cordlike or bead-like formations resembling thrombophlebotic indurations. The nodules may disappear by resorption without leaving a scar but usually the overlying structures become involved and larger infiltrated patches are formed. This stage may be similar to the starting phase of the afore-

mentioned perivenous pachyderma. The nodules inside the plaques tend toward superficial necrosis, resulting in deep punched-out circular ulcers with clearcut borders or in irregular superficial cavities with undermined edges, always with some degree of infiltration and purplish discoloration at the borders. This induration at the periphery is not so frequently observed in thrombophlebotic ulcers. Healing in erythema induratum is accompanied with the appearance of round depigmented cicatricial areas with hyperpigmentation at the borders.

Erythema induratum is generally considered to be of a tuberculous nature. Confirmation will be found in the usual presence of a tuberculous focus in the patient, in the positive reaction to tuberculin in all dilutions and in the coexistence of papulonecrotic tuberculids. But some authors refute the causative relationship of tuberculosis to erythema induratum. Telford,<sup>15</sup> for instance, expressed the opinion that Bazin's disease is not tuberculous and is in no way different from erythrocyanosis. The two diseases may occur in the same position on a fat and cyanotic leg when the limb is exposed to cold, and their clinical courses are exactly the same. Other authors, including O'Leary,<sup>16</sup> regard disease of the blood vessels, probably of the veins, as a significant factor in the cause of erythema induratum. The quick response of symptoms to the application of Parí rubber bandages has been stressed by O'Leary as proof for this theory. According to my experience, the weak peripheral circulation is only a predisposing factor for the development of erythema induratum in women and girls who are obliged to stand a great deal. In the same way concomitant varicosities may increase the tendency to recurrent outbreaks. The nearly symmetric distribution over the legs, the clinical course, the morphologic features and, finally, the histologic observations are sufficient to distinguish erythema induratum from chilblain affections and from all phlebitis-like nodular inflammations about the veins of the limbs.

Erythema nodosum may occasionally simulate the patchy form of phlebitis. It may also resemble erythema induratum, but the outer aspects of the limbs are preponderantly affected and the eruptions run a more acute course. Erythema nodosum does not end in ulceration, and there is no scarring or depression after regression of the nodules.

15 Telford, E. D. Lesions of the Skin and Subcutaneous Tissue in Diseases of the Peripheral Circulation, *Arch Dermat & Syph* 36 952 (Nov) 1937.

16 O'Leary, P. A., in discussion on Ebert, M. H. Case for Diagnosis (Erythema Induratum), *Arch Dermat & Syph* 48 343 (Sept) 1943.

14 Biegeleisen, H. I. Lymphedema Occurring with Varicose Veins, *Arch Dermat & Syph* 33 689 (April) 1936.

### VARICOSE ULCERATIONS OF THE LEG AND THEIR DIFFERENTIATION

The morphologic features of cutaneous ulcerative lesions of the legs are as variable and diversified as their underlying pathologic conditions. According to McPheeters<sup>17</sup> and Ochsner,<sup>18</sup> the defective return circulation is the main causative factor for nearly 80 per cent of the ulcers. Other investigators deny the relationship between ulcerations of the limbs and the impaired venous circulation. For instance, Becker<sup>19</sup> found that many patients with ulcers of the leg do not have varicose veins and most of the patients with varicose veins do not have ulcers. Different factors have to be taken into consideration in defining the cause of chronic ulcerative lesions of the limbs.

The detection of varicosities may occasionally be difficult. In some instances venous valvular insufficiency may be present without obvious change of thickness and form of the vein. However, palpation and percussion tests and the Trendelenburg test may prove the incompetence of the veins.<sup>20</sup> Furthermore, the varicosities may be hidden in stout persons or in patients with swollen limbs. In order to bring these varicose trunks into prominence, bandaging or rest in bed will be found useful. In other cases the varicose state is limited to deeper-seated small or medium-sized veins which form a network of dilated communicating branches and which are not recognized by direct observation. Phlebography may reveal these deep venous channels.<sup>21</sup> Occasionally in persons with perivenous pachyderma the originally distended veins shrink to sclerotic cords which may be found by deep palpation. The connection of some ulcers, such as "phlebotic ulcers," with the deficient venous circulation may be overlooked, since their formation takes place five or even ten years after subsidence of acute symptoms, but an accurate history will diminish the margin of error. The development of varicose ulcers generally depends on the type and severity of the varicosities and the occupation of the patient. Trauma or

a minimal infection from scratching are sufficient to initiate extensive and long-lasting ulcerations. Profuse bleeding of superficial varicosities may be the preliminary symptom of ulcers in the region of the ankle.

The close association of ulcerative lesions with varicosities can easily be traced when so-called feeder or key veins arise in their neighborhood (fig 6). Soft elevations representing venous pools may be felt beneath or adjacent to the ulcers, or the draining veins may become noticeable only after complete healing of the cavities. There are usually dermatitis and pigmentation



Fig 6—Varicose ulcers with feeding varicose veins

at the periphery of the ulcers. Chronic inflammatory changes may occasionally extend to the periosteum and even to the bones. Onychogryphosis may be symptomatic of the chronic inflammation.

Constitutional disorders may influence the shape and duration of ulcers of the leg in older people. De Takats<sup>22</sup> observed that 50 per cent of his patients with varicose veins also showed

17 McPheeters, H O, and Anderson, J K. Injection Treatment of Varicose Veins and Hemorrhoids, ed 2, Philadelphia, F A Davis Co, 1943.

18 Ochsner, A, and Mahorner, H. Varicose Veins, St. Louis, C V Mosby Company, 1939.

19 Becker, S W, and Obermayer, M E. Modern Dermatology and Syphilology, Philadelphia, J B Lippincott Company, 1943, p 277.

20 McCallig, J J, and Heyerdale, W W. A Basic Understanding of Varicose Veins, J A M A **115** 97 (July 13) 1940.

21 DeBailey, M, Schroeder, G F, and Ochsner, A. Significance of Phlebography in Phlebothrombosis, J A M A **123** 738 (Nov 20) 1943.

22 de Takats, G, Quint, H, Tillotson, B I, and Crittenden, P J. The Impairment of Circulation in the Varicose Extremity, Arch Surg **18** 671 (Feb) 1929.

diminished arterial supply, which is partly responsible for the decreased resistance of the tissues to trauma. The preponderance of arteriosclerotic changes over involvement of the veins can be proved by tests like the Samuel postural test, palpation of the pulse, a roentgenogram of the arteries and oscillometric readings. Nephritis, heart disease or cirrhosis of the liver may be contributing factors to the chronic engorgement of the legs.

Diagnostic problems may arise if the typical features of the varicose ulcerations become changed by other concomitant pathologic states. The most common ulcers to be distinguished from varicose ulcers are syphilitic ulcerations of the tertiary stage<sup>23</sup>. Tuberculous, malignant and mycotic ulcerative lesions must be excluded. Gangrenous pyoderma and ecthyma, ulcers due to ingestion of drugs and ulcers associated with sickle cell anemia and idiopathic colitis should be recognized. Tropical ulcers, Gallipoli sore,<sup>24</sup> yaws and leishmaniasis must also be considered in the differential diagnosis of varicose ulcerations.

The correct interpretation of all these chronic ulcerations of the leg and the recording of evidence disclosing their underlying causative factors are of preeminent importance.

<sup>23</sup> Ochsner, A. Chronic Cutaneous Ulceration of the Lower Extremities, New Orleans M & S J 84 594 (Feb) 1932.

<sup>24</sup> Vischer, A. L. Das Wustengeschwür, Schweiz med Wchnschr 72 1436 (Dec) 1942,

#### SUMMARY AND CONCLUSIONS

The close connection of cutaneous and subcutaneous lesions of the legs with the deficient venous circulation is often overlooked. Aggravation of symptoms corresponds to the progressive impairment of the venous circulation and the relationship may be confirmed by the quick response of cutaneous manifestations to the elimination of degenerated venous channels. Correct interpretation and differentiation of cutaneous changes caused by hemostasis may be facilitated by tests for incompetency of the veins and by infra-red photography or by phlebography. A roentgenogram of the veins will help to prevent the diagnosis of deep phlebitis in various diseases of the legs of obscure origin.

Extensive fibromatosis of the legs, which is a characteristic feature of "perivenous pachyderma," may be occasionally encountered after deep phlebitis. The fibrotic state in both diseases may be explained by the chronic damage to the venous and lymph channels and by reactive hyperplastic tissue changes about the vessels. Ulcerations developing in the two conditions are much alike.

Chronic ulcerative lesions of the legs are caused in nearly 80 per cent of cases by varicosities. The deficient venous circulation may be regarded as a contributing factor in the development of certain cutaneous diseases of the legs, as, for instance, erythema induratum.

969 Park Avenue

## DERMATITIS VENENATA

### FOLLOWING USE OF PENICILLIN OINTMENT

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It has been previously noted that penicillin when administered parenterally gives rise to varied cutaneous manifestations,<sup>1</sup> such as urticaria, recurrent vesicular eruptions and exfoliative dermatitis. A case of contact dermatitis<sup>2</sup> has been reported in a medical officer who was preparing penicillin.

To these cases of penicillin sensitivity I shall add a case of dermatitis venenata which developed in a white man following treatment for mild conjunctivitis with penicillin ointment.

#### REPORT OF A CASE

The patient was admitted to the sick list at another hospital complaining of swelling about the eyes and face. The onset was three weeks before, when he noted a slight burning and irritation of the eyes, but no accompanying redness or injection. A diagnosis of mild conjunctivitis was made.

He was given some eye drops for a couple of days, without relief of symptoms. He then used a 5 per cent sulfathiazole ointment for ten days, but there was still no change in his condition. Then a penicillin ointment

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1 Moore, J. E., Mahoney, J. F., Schwartz, W., and Sternberg, T. Treatment of Early Syphilis with Penicillin, *J. A. M. A.* **126** 67 (Sept 9) 1944. Mahoney, J. F., Arnold, R. C., Sterner, B. L., Harris, A., and Twalley, M. R. Penicillin Treatment of Early Syphilis, *ibid.* **126** 63 (Sept 9) 1944. Stokes, J. H., Sternberg, T. H., Schwartz, W. H., Mahoney, J. F., Moore, J. E., and Wood, W. B. The Action of Penicillin in Late Syphilis, *ibid.* **126** 79 (Sept 9) 1944. Graves, W. N., and Carpenter, C. C. Recurrent Vesicular Eruptions, *Arch. Dermat. & Syph.* **50** 6 (July) 1944.

2 Pyle, H. D., and Rattner, H. Contact Dermatitis from Penicillin, *J. A. M. A.* **125** 903 (July 9) 1944.

was placed in his eyes, and on the following morning the patient noticed edema of the eyelids and surrounding tissue. The ointment was discontinued for one day and then reapplied, with more severe edema and erythema about the eyes and upper part of the face resulting.

On Feb 12, 1945 the patient was transferred to this hospital with the history given. Results of examination were essentially negative except for edema and an erythematovesicular dermatitis of the eyelids and the entire periorbital region, extending down to the lower end of the nose and cheeks. There was a slight purulent discharge in the palpebral fissures. Conjunctivas, scleras and corneas appeared normal.

A diagnosis of dermatitis medicamentosa was made. Medication was stopped, and compresses of boric acid solution were applied every hour. Sodium thiosulfate, 1 Gm., was administered intravenously. The dermatitis regressed with great rapidity, and the patient was discharged as cured on February 19. He returned to his original place of duty, where, at my request, patch tests were made with the sulfathiazole and penicillin ointments previously employed. These tests were applied to the patient's back on February 23,<sup>3</sup> and were removed twenty-four hours later. There was a negative reaction to the sulfathiazole. The area tested with the penicillin ointment showed an erythematous, vesicular eruption, the size of a half dollar, surrounded by a zone of edema. This was associated with some burning and itching which lasted for three days. After seven days there was still some scaling of the skin in that area. The eyelids and surrounding tissues were not affected. Many other patients have been treated with the ointment used on this patient, and no reactions have been observed. Unfortunately the patient was transferred to another activity before he could be tested with the various components of the ointment bases, which in each preparation were: wool fat 5 per cent, white wax 5 per cent and white petrolatum 90 per cent.

#### SUMMARY

A case of dermatitis venenata of the eyelids and face following the use of penicillin ointment is reported.

3 Carr, R. M. Personal communication to the author.

# NEW CUTANEOUS BACTERICIDAL AGENT USED IN SOAP

## FURTHER PRACTICAL STUDIES

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In a recent study<sup>1</sup> we investigated the cutaneous bactericidal properties of 2,2'-dihydroxy-3,5,6-3'5', 6'-hexachlorodiphenylmethane<sup>2</sup> (hereinafter termed G-11) when incorporated in a toilet soap to the amount of 2 per cent,<sup>3</sup> and found that the routine daily use of this germicidal soap made it possible to reach and maintain an exceedingly low bacterial population on the skin of the hands and forearms. We especially wish to direct attention to the fact that this result can be achieved only by using G-11, or some other equally effective germicide, in a soap or other suitable detergent that is used exclusively by the individual each and every time he has any occasion to use soap for any purpose whatsoever. We stress this point particularly because since our recent publication<sup>1</sup> we have been deluged with requests for information concerning soap to be used for operating room scrub-up. G-11 soap is effective for this purpose *only if it is exclusively used* by the surgeon every time he uses soap and water for each and every washing. This important principle had apparently not been thoroughly understood. Conducting our investigations according to a method modified<sup>4</sup> after those of Price,<sup>4</sup> Pohle and Stuart,<sup>5</sup> and Pillsbury<sup>6</sup> and

others, we compared the effect of this agent with 70 per cent (by weight) alcohol, a commercial soap claimed to be germicidal (neko) and a standard surgical scrub-up technic, by hand washing experiments on a large scale. This study included experiments which showed that G-11 was nonirritating to the human skin, as shown by over four hundred individual patch tests.

We are herewith reporting on additional experiments designed to prove that 2 per cent G-11 soap had produced a truly bactericidal rather than bacteriostatic action and that it does not form a film on the skin under which viable bacteria are retained in large numbers. The effect of G-11 soap on pathogenic cutaneous organisms was also included in this study.

### QUESTION OF FILM FORMATION

Miller and his associates<sup>7</sup> have shown by experiments that washing the hands with the use of a germicidal cationic detergent such as zephiran chloride leaves the skin apparently free from bacteria, but subsequent washings with an anionic soap releases large numbers of live bacteria, thus suggesting the presence of an imperceptible film of the cationic substance. Alcohol, alum and mercuric salts have also been observed to produce protective films masking viable organisms.

We reasoned that if a film formed by a cationic soap is broken by the use of an anionic soap, the opposite should also take place. Therefore, if anionic soap containing compound G-11 would form a film on the skin, then this film should be removable by subsequent use of a cationic soap, and this should result in a flora

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Read at the Sixty-Fifth Annual Meeting of the American Dermatological Association, Inc., Chicago, June 20, 1944

1 Traub, E. F., Newhall, C. A., and Fuller, J. R. Studies on the Value of a New Compound Used in Soap to Reduce the Bacterial Flora of the Human Skin, *Surg., Gynec. & Obst.* **79** 205, 1944

2 William S. Gump, U. S. Patent 2,250,480

3 The soaps used in these experiments were supplied by Givaudan-Delawanna, Inc., New York

4 Price, P. B. The Bacteriology of Normal Skin, *J. Infect. Dis.* **63** 301, 1938, New Studies in Surgical Bacteriology and Surgical Technic, with Special Reference to Disinfection of Skin, *J. A. M. A.* **111** 1993 (Nov. 26) 1933

5 Pohle, W. D., and Stuart, L. S. The Germicidal Activity of Rosin Soap and Fatty-Acid Soap as Indicated by Hand Washing Experiments, *Oil and Soap*, **18** 2, 1941. The Germicidal Action of Cleansing Agents, *J. Infect. Dis.* **67** 275, 1940

6 Pillsbury, D. M., Livingood, C. S., and Nichols, A. C. Bacterial Flora of the Normal Skin. Report on Effect of Various Ointments and Solutions, with Comments on Clinical Significance of This Study, *Arch. Dermat. & Syph.* **45** 61 (Jan.) 1942

7 Miller, B. F., Abrams, R., Huber, D. A., and Klein, M. Formation of Invisible, Nonperceptible Films on Hands of Cationic Soaps, *Proc. Soc. Exper. Biol. & Med.* **54** 254, 1943

of normal numbers We set up an experiment on this basis

Six subjects washed through the standard ten-basin washing procedure, using control soap (anionic) Three of the subjects substituted Onyxsan S 1 per cent (a surface active agent of the alkyl amidoalkyl amidoazoline type) and the remaining 3 subjects zephiran chloride 1 per cent in basin 5 for the control soap Onyxsan S and zephiran chloride are cationic detergents, the former is nonbactericidal, while the latter is a potent germicide The results are shown in table 1

TABLE 1—Number of Organisms on Skin After Use of Anionic Control Soap and Cationic Detergent

Cationic detergent was used in basin 5, anionic control soap used in all other basins Subjects I, II and III used zephiran chloride, and subjects IV, V and VI used Onyxsan S in basin 5

| Subjects | Basin |     |     |     |     |     |     |     |    |    |
|----------|-------|-----|-----|-----|-----|-----|-----|-----|----|----|
|          | 1     | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9  | 10 |
| I        | 883   | 741 | 224 | 244 | 6   | 229 | 132 | 128 | 64 | 64 |
| II       | 475   | 302 | 174 | 228 | 1   | 68  | 53  | 82  | 90 | 86 |
| III      | 262   | 154 | 98  | 80  | 7   | 66  | 38  | 39  | 28 | 25 |
| IV       | 85    | 126 | 101 | 98  | 411 | 65  | 78  | 46  | 42 | 37 |
| V        | 653   | 523 | 133 | 403 | 393 | 133 | 113 | 96  | 76 | 56 |
| VI       | 825   | 418 | 333 | 331 | 484 | 313 | 152 | 94  | 95 | 69 |

Actual counts per basin may be obtained by multiplying the numbers by 10,000

In a second experiment 6 subjects washed through the standard ten-basin washing procedure, using control (anionic) soap and each subject was given a bar of 2 per cent G-11 (anionic) soap with instructions to use only this soap for all washings of the skin for the following week and then to return for the final washings The final washings were conducted as follows

Three subjects washed for a two minute period, using a 1 per cent aqueous solution of Onyxsan S, and rinsed in basin 1 Washing with control (anionic) soap then followed in the other nine basins The remaining 3 subjects went through this same routine, except that 1 per cent zephiran chloride was used instead of Onyxsan S The results are shown in table 2 and the chart

TABLE 2—Number of Organisms on Skin After Use of G-11 for a Week

Cationic detergent was used in a two minute washing prior to basin 1 Subjects I, II and III used zephiran chloride and subjects IV, V and VI used Onyxsan S, 2 per cent G-11 (anionic) soap had been used by all subjects routinely for one week previously

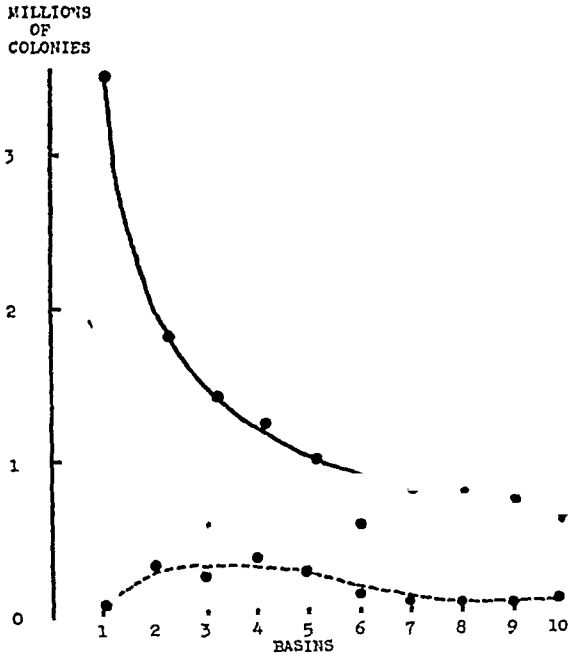
| Subjects | Basin |    |    |     |    |    |    |    |    |    |
|----------|-------|----|----|-----|----|----|----|----|----|----|
|          | 1     | 2  | 3  | 4   | 5  | 6  | 7  | 8  | 9  | 10 |
| I        | 0     | 15 | 21 | 13  | 18 | 11 | 3  | 9  | 2  | 12 |
| II       | 0     | 91 | 93 | 90  | 63 | 48 | 38 | 18 | 24 | 27 |
| III      | 2     | 9  | 8  | 7   | 3  | 6  | 2  | 2  | 1  | 1  |
| IV       | 1     | 8  | 2  | 4   | 2  | 7  | 1  | 4  | 1  | 3  |
| V        | 1     | 91 | 60 | 115 | 79 | 47 | 38 | 35 | 44 | 71 |
| VI       | 17    | 9  | 12 | 6   | 7  | 2  | 5  | 5  | 5  | 4  |

Actual counts per basin may be obtained by multiplying the numbers by 10,000

Referring to table 1, there will be noted an obvious difference in the action of zephiran chloride and Onyxsan S It would appear that zephiran chloride kills those bacteria which are removed in basin 5, but, as is shown, the count returns to a high level as soon as the cationic film is removed by anionic soap in basins 6 to

10 Thus zephiran chloride apparently has only a superficial action and simply covers the bacteria temporarily with a removable film These results agree with the findings of Miller and his associates<sup>7</sup> Onyxsan S, which is nongermicidal, has an action similar to that of the ordinary anionic soaps After G-11 (anionic) soap is used for one week, it does not matter whether zephiran chloride or Onyxsan S is used before the final washing (table 2) The counts are equally low and not higher than in the previous experiments, in which no cationic detergent was applied prior to the washings with control soap

Obviously, if our premise is correct, G-11 does not exert its apparent action in reducing the resident bacterial flora of the skin by obscuring the bacteria beneath a film This substantiates the



Results of experiments The unbroken line shows results when control (anionic) soap was used in all basins The broken line shows results of final washings when subjects had used 2 per cent G-11 soap for one week Cationic soap "film removing detergent" was used in basin 1, control soap was used in the last nine basins

opinion that G-11 acts by actually killing the bacteria on and in the skin, in other words, 2 per cent G-11 soap does not produce a protectant film on the skin, a condition which would give rise to a false sense of security

THE ROLE OF BACTERIOSTASIS

We felt certain that any trace of G-11 soap left on the skin following its routine use over one week and possibly carried over in the rinsings obtained from control soap washings would be so negligible that it could exert no bacteriostatic effect in the still more dilute cultures made from these rinsings



However, in order to prove this point conclusively, cultures were made of the rinsings obtained in the control soap washings after the routine use of 2 per cent G-11 soap for one week, by plating 1 cc and 0.1 cc samples from each basin. These results are shown in tables 3, 4, 5 and 6. If bacteriostasis is not a factor, then the ratio of the number of colonies obtained in these two plates should be of the order of 10:1. If G-11 carried over does cause bacteriostasis in a certain dilution, then the bacteriostasis should be lessened by increasing the dilution of G-11.

TABLE 3—Control Soap Washings Prior to Routine Use of 2 per Cent G-11 Soap

| Subjects | Size of Sample | Basins |     |     |     |     |     |     |     |     |     |
|----------|----------------|--------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|          |                | 1      | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  |
| I        | 0.10 cc        | 327    | 276 | 260 | 179 | 252 | 171 | 158 | 172 | 113 | 125 |
|          | 0.01 cc        | 35     | 43  | 25  | 21  | 14  | 22  | 17  | 18  | 15  | 11  |
| II       | 0.10 cc        | 141    | 200 | 166 | 140 | 81  | 78  | 79  | 162 | 53  | 52  |
|          | 0.01 cc        | 15     | 21  | 19  | 18  | 8   | 10  | 9   | 5   | 2   | 8   |

Actual counts per basin may be obtained by multiplying counts as shown by 20,000 for the 0.1 cc samples and by 200,000 for the 0.01 cc samples.

TABLE 4—Control Soap Washings Following a Week's Routine Use of 2 per Cent G-11 Soap

| Subjects | Size of Sample | Basins |     |    |    |    |    |    |    |    |     |
|----------|----------------|--------|-----|----|----|----|----|----|----|----|-----|
|          |                | 1      | 2   | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10  |
| I        | 1.00 cc        | 86     | 1   | 41 | 25 | 27 | 23 | 11 | 17 | 13 | 101 |
|          | 0.10 cc        | 13     | 0   | 3  | 4  | 1  | 3  | 5  | 0  | 1  | 14  |
| II       | 1.00 cc        | 126    | 105 | 96 | 92 | 46 | 43 | 22 | 23 | 21 | 16  |
|          | 0.10 cc        | 10     | 17  | 11 | 8  | 5  | 2  | 2  | 3  | 5  | 4   |

Actual counts per basin may be obtained by multiplying counts as shown by 2,000 for the 1 cc samples and by 20,000 for the 0.1 cc samples.

The series of ten basins for each subject has been added together in order to simplify the foregoing findings.

TABLE 5—Control Soap Washings Prior to Routine Use of 2 per Cent G-11 Soap

Figures show total number of colonies of all basins added together.

| Subjects | Grand Total Counts |         | Ratio  | Average Ratio |
|----------|--------------------|---------|--------|---------------|
|          | 0.1 Cc             | 0.01 Cc |        |               |
| I        | 2,028              | 221     | 10:1.1 | 10:1.1        |
| II       | 1,142              | 125     | 10:1.1 |               |

TABLE 6—Control Soap Washings Following a Week's Routine Use of 2 per Cent G-11 Soap

Figures show total number of colonies of all basins added together.

| Subjects | Grand Total Counts |        | Ratio  | Average Ratio |
|----------|--------------------|--------|--------|---------------|
|          | 1 Cc               | 0.1 Cc |        |               |
| I        | 345                | 44     | 10:1.3 | 10:1.2        |
| II       | 650                | 76     | 10:1.1 |               |

Therefore, if we can obtain counts of the same ratio regardless of the dilution bacteriostasis is not involved.

It is readily seen in table 6 that the ratio obtained in the two dilutions after the routine use of 2 per cent G-11 soap is approximately the same as the ratio obtained in the two dilutions prior to the use of the 2 per cent G-11 soap.

The remote possibility that the extremely small amount of compound G-11 which could be carried over from the skin to the basins and then to the cultures exerts a bacteriostatic action is entirely excluded by these findings, hence the low counts obtained in control soap washings following the routine use of 2 per cent G-11 soap are not due to bacteriostasis.

#### EFFECT ON PATHOGENS

The question had been brought up as to whether 2 per cent G-11 soap kills the pathogenic portions of the cutaneous flora as well as the non-pathogenic organisms. We have attempted to answer this question by a procedure using *Staphylococcus aureus* as an example of the pathogenic flora. Because *Staph aureus* is usually found on 10 per cent of human skins, because it is an accepted organism in evaluating the potency of germicides, and because of the relative ease with which it is identified, we decided to use its disappearance from the cutaneous surface as an indicator of effectiveness of G-11 soap on pathogens.

Accordingly, the skin on the dorsa of the hands of 207 industrial employees was swabbed to obtain carriers of *Staph aureus*. *Staph aureus* was identified as such by finding several colonies of a gram-positive coccus which produces a golden pigment, hemolyzes blood agar and gives a positive reaction to the coagulase test. From 8 persons who were found to be carriers of *Staph aureus* at the first swabbing cultures were taken at intervals of at least one week in order to establish definitely a carrier state, and they were then given bars of 2 per cent G-11 soap to use in all washings for a period of ten days. Any subject on whom *Staph aureus* could be found on at least two of the three swabbing dates prior to the routine use of 2 per cent G-11 soap was considered a proved carrier. The skin of these persons was again swabbed two times after the routine use of G-11 soap was ended, and cultures were made to determine the presence or absence of *Staph aureus*. The results are shown in table 7.

It is interesting to note that subject 47 ran out of 2 per cent G-11 soap three days before the swabbing on August 11 was done. It is possible that he reestablished his pathogenic flora during

this interval A study of table 7 shows that 2 per cent G-11 soap was effective in removing Staph aureus in 7 out of 8 cases of proved carriers This suggests an efficiency of 87 5 per cent and warrants the assumption that the

TABLE 7—Presence or Absence of Staph Aureus on Skin of Carriers After Routine Use of G-11 Soap

| Subject | 5/19 | 7/13 | 8/1 |          | 8/11 | 8/22 |
|---------|------|------|-----|----------|------|------|
| 202     | +    | +    | —   | All      | —    | +    |
| 86      | +    | —    | +   | subjects | —    | +    |
| 89      | +    | —    | +   | used     | —    | +    |
| 174     | +    | —    | +   | 2% G 11  | —    | —    |
| 165     | +    | +    | +   | soap     | —    | +    |
| 118     | +    | +    | —   | during   | —    | —    |
| 47      | +    | +    | —   | this     | +    | +    |
| 195     | +    | +    | +   | interval | —    | +    |

routine use of 2 per cent G-11 soap is equally effective in removing pathogenic and nonpathogenic bacteria from the human skin

SUMMARY AND CONCLUSIONS

1 Two per cent dihydroxyhexachlorodiphenyl methane (G-11) incorporated in toilet soap enabled the subjects studied to maintain an exceedingly low bacterial population on the skin of the hands and forearms

2 Compound G-11 was nonirritating to the skin as judged by more than four hundred patch tests These were repeated on the same subjects after ten to fourteen days and were again found to be negative, showing that no sensitivity of the skin had been produced by the first tests Subjects using 2 per cent G-11 soap regularly for one year have shown no evidence of irritation

3 Our hand washing experiments (121 individual series of washings) indicate that the most significant results were obtained by the regular daily routine use of 2 per cent G-11 soap The evidence indicates that the exclusive use of toilet soap containing compound G-11 in a concentration of 2 per cent has such an effect on the bacterial flora of the human skin that the so-called resident bacteria are decidedly and permanently (as long as this soap is used) exclu-

sively reduced in number A person using this soap regularly each time his hands are washed has a lower resident count after two minutes of washing than one who washes for twenty minutes with ordinary toilet soap The striking bactericidal effects obtained by daily use of toilet soap containing compound G-11 compared with regular use of ordinary or control soap and neko soap, a commercial soap claimed to be germicidal, indicate its value

4 These results lead us to conclude that the daily and exclusive use of a soap containing compound G-11 would enable a surgeon or operating room attendant to maintain an extremely low resident bacterial population on his skin

5 Experiments prove that 2 per cent G-11 soap does not form a film which would retain a large number of live bacteria beneath it

6 The remarkably lowered resident flora following the routine use of 2 per cent G-11 soap has not resulted from bacteriostasis but from actual killing

7 Two per cent G-11 soap when used exclusively is an efficient agent in reducing the number of both pathogenic and nonpathogenic organisms found on the human skin

8 Exclusive use of soap containing compound G-11, according to our experiments, should reduce the probability of infection following abrasions and superficial wounds of the skin This point might be of value in the hygienic care of members of the armed forces Attendants of wounded in front line areas where lengthy surgical scrub-up routines which include the use of alcohol and iodine may be out of the question could nevertheless feel that the resident bacterial populations on their hands were at an exceedingly low level

9 The use of G-11 either in soap or in other vehicles for protection against cutaneous infections from barber shops and beauty parlors, hair follicle infections from cutting oils, etc, is suggested

# DERMATITIS MEDICAMENTOSA ASSOCIATED WITH SECONDARY POLYCYTHEMIA

## REPORT OF A CASE

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LOS ANGELES

Polycythemia is known to occur as a disease entity of unknown cause, primary polycythemia,<sup>1</sup> and as a relative or symptomatic transient disorder of the red blood cells secondary to various diseases. Primary polycythemia has been described as associated with deep pruritic infiltrative cutaneous lesions and a generalized papular eruption (*acne urticata polycythaemica*)<sup>2</sup>. No record, however, could be found in the dermatologic literature of the association of symptomatic or relative polycythemia with a dermatologic disease. The following case is therefore reported as an example of symptomatic or secondary polycythemia associated with a cutaneous disease, dermatitis medicamentosa.

## REPORT OF CASE

*History*—N. J., an 18 year old Jewish clerk, was first seen on Aug. 9, 1943, because of a generalized red itching eruption. The history revealed that one week previously he had received a subcutaneous injection of procaine hydrochloride and zylcaine as local anesthetics during the surgical treatment of external hemorrhoids. No other drugs were administered. Twenty-four hours after the injection a fine red itching rash appeared on the face. The eruption became more pronounced and pruritic during the next three days and spread to the neck, trunk and extremities. The pruritus was intense and the face, neck and upper part of the chest became noticeably swollen and indurated. Discrete red papules and papulovesicles appeared on the cheeks. The face became so swollen that the patient had difficulty in opening his eyelids and mouth. He stated that when he was 11 years old he had a severe local and febrile reaction following the administration of tetanus toxin-antitoxin.

*Physical and Dermatologic Examinations*—The physical examination revealed normal conditions. The heart rate was 120, and the blood pressure was 125 systolic.

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1 Vaquez, H. Sur une forme speciale de cyanos s'accompagnant d'hyperglobulie excessive et persistente, *Compt rend Soc de biol* 4 384, 1892. Osler, W. Chronic Cyanosis with Polycythemia and Enlarged Spleen. A New Clinical Entity, *Am J M Sc* 126: 187, 1903.

2 Gans, O. The Skin Picture in Hematopoietic Diseases, *Arch Dermat & Syph* 16 4 (July) 1927. Klunder, J. V. Acne Urticata Polycythaemica, *ibid* 38 145 (July) 1938.

and 80 diastolic. The temperature was 101.5 F. The dermatologic examination revealed that the face, neck, trunk and extremities were covered with a bright erythematous macular and papulovesicular eruption. The face, neck and upper part of the chest were swollen and enlarged to about twice normal size. The swelling was so intense that the eyelids were tightly shut and the mouth could be opened only with difficulty. The facial features were distorted, and the skin of the swollen areas felt hard and indurated.

*Laboratory Examination*—The examination of the urine showed a positive reaction for acetone. The serologic reaction of the blood for syphilis was negative. The examination of the blood on August 9 showed hemoglobin content, 122 per cent (20.6 Gm); erythrocytes, 6,930,000 per cubic millimeter, color index, 0.88, and leukocytes, 11,800 per cubic millimeter, with 86.5 per cent neutrophils, 15 per cent eosinophils, 8 per cent lymphocytes and 4 per cent monocytes.

On August 11 the hematologic examination showed hemoglobin content, 104 per cent (17.6 Gm), erythrocytes, 5,800,000 per cubic millimeter, color index, 0.91, and leukocytes, 8,900 per cubic millimeter, with 78 per cent neutrophils, 16 per cent lymphocytes, 4 per cent eosinophils and 2 per cent monocytes.

On August 17 the hematologic examination showed hemoglobin content, 85 per cent (14.5 Gm), erythrocytes, 5,180,000 per cubic millimeter, color index, 0.82, and leukocytes, 10,200 per cubic millimeter, with 68 per cent neutrophils, 23 per cent lymphocytes, 2 per cent eosinophils and 7 per cent monocytes.

*Course*—After the initial examination, the swelling and induration of the face, neck and chest became greater for two days and then subsided entirely within one week. The facial features became normal, and the generalized pruritic eruption disappeared. The temperature varied from 101.5 to 100 F, and the pulse rate varied from 120 to 90 until the lesions subsided.

*Treatment*—The treatment consisted in the application of cold compresses of dilute (1:16) solution of aluminum subacetate to the face and neck and of an antipruritic shake lotion to the trunk and extremities. Calcium gluconate, 15½ grains (1 Gm), and 50 cc of 50 per cent solution of dextrose were administered intravenously daily.

## COMMENT

Symptomatic polycythemia, or erythrocytosis, must be differentiated from primary polycythemia. Primary polycythemia is an idiopathic disease of unknown cause associated with an absolute increase in the erythrocytes per cubic millimeter and an increase in the total red blood cell count. Symptomatic polycythemia, or erythrocytosis, is a transient disorder in which the total number of

erythrocytes is normal although the number of red blood cells per cubic millimeter is increased. Relative or secondary increases in the number of erythrocytes are caused by a decrease in the plasma volume. This may result from fluid lost by the blood during various conditions, such as excessive perspiration and ventilation of the lungs (exercise), profuse diarrhea and severe vomiting. The action of bacterial and chemical toxic agents on the red blood cells and congenital heart disease may also cause secondary polycythemia. Among the chemical agents reported to cause polycythemia are tuberculin, epinephrine, digitalis, carbon monoxide, arsenic, caffeine and opium. No reference was found in the medical literature to symptomatic or relative polycythemia associated with procaine hydrochloride or zylcaine dermatitis. There is also no record of symptomatic polycythemia associated with the loss of plasma from the blood in cases of severe edema and inflammation of the skin and subcutaneous tissues due to a cutaneous disease, dermatitis medicamentosa. Zylcaine is a combination in purified peanut oil of local anesthetics, consisting of a procaine base, 1.5 per cent, butyl aminobenzoate, 6 per cent, and benzyl alcohol, 5 per cent.

Symptomatic, or secondary, polycythemia is a transitory condition, and definite improvement occurs by dilution of the blood with fluid or by

reabsorption of the lost blood plasma in edematous areas, as in our patient's dermatosis. It is debatable whether the drug or drugs causing the dermatitis in our patient had any direct toxic action on the red blood cells. It is our belief that the secondary polycythemia was caused by an excessive loss of blood plasma associated with the severe edema and swelling and inflammation of the skin and subcutaneous tissues of our patient's face, neck and chest resulting from dermatitis medicamentosa.

#### SUMMARY AND CONCLUSIONS

A patient was encountered with dermatitis medicamentosa associated with secondary polycythemia.

Secondary polycythemia associated with dermatologic diseases can be caused by severe edema, swelling and inflammation of the skin and subcutaneous tissues resulting in decided loss of blood plasma.

Secondary polycythemia associated with a dermatologic disease, such as dermatitis medicamentosa, is a transitory condition that disappears when the edema and swelling of the skin and subcutaneous tissues clear.

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# WATERHOUSE-FRIDERICHSEN SYNDROME

## REPORT OF A CASE

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The disease known as the Waterhouse-Friderichsen syndrome was described as an entity by Graham Little<sup>1</sup> in 1901. He reviewed the literature and published 4 cases of his own. Waterhouse<sup>2</sup> reported his case in 1911 and reviewed 15 others. He gave an accurate description of symptomatology and pathology.

In 1918 Friderichsen,<sup>3</sup> in Germany, published his 2 cases and brought the literature up to date. There was little information as to the cause of the syndrome at this time. MacLagan and Cooke,<sup>4</sup> in 1916, were perhaps the first to label the meningococcus as the etiologic agent. Reports have been printed in the German literature concerning the entity by Baumann<sup>5</sup> and others. Aegerter<sup>6</sup> and Sacks<sup>7</sup> reviewed the literature in 1936 and 1937 respectively. Considerable publicity has been given to the syndrome during the last three to four years. Recent papers by Bush and Bailey<sup>8</sup> and Boger<sup>9</sup> have presented the current and up-to-date features of this entity.

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5 Baumann, T. Zur Aetiologie und Klinik der akuten Nebenniereninsuffizienz (Nebennierenblutungen und Hypoplasie), *Ztschr f Kinderh* 51:276-293, 1931.

6 Aegerter, E F. The Waterhouse-Friderichsen Syndrome. A Review of the Literature and Report of Two Cases, *I A M A* 106:1715-1719 (May 16) 1936.

7 Sacks, M S. Fulminating Septicemia Associated with Purpura and Bilateral Adrenal Hemorrhage (Waterhouse-Friderichsen Syndrome). Report of Two Cases with Review of the Literature, *Ann Int Med* 10:1105-1114 (Feb) 1937.

8 Bush, F W, and Bailey, F R. The Treatment of Meningococcus Infections with Special Reference to the Waterhouse-Friderichsen Syndrome, *Ann Int Med* 20:619-631 (April) 1944.

9 Boger, W P. Fulminating Meningococcemia. Demonstration of Intracellular and Extracellular Meningococci in Direct Smears of the Blood, *New England J Med* 231:385-387 (Sept 14) 1944.

The history, symptoms and sequence of events are so frequently repeated that the Waterhouse-Friderichsen syndrome is a definite entity. Most of the cases are usually seen in children under the age of 2 years. It is not infrequent in adults.

The characteristic clinical history usually states that the patient was well until the sudden attack of the disease. The early symptoms are nonspecific, and are those that might occur in any acute infection.

The first symptoms may be malaise, restlessness, chills, headaches or vomiting. Abdominal pain occurs in a high percentage of cases. There is hyperpyrexia of spiking septic type, with a temperature as high as 107 F. The patient soon becomes stuporous and lethargic and convulsions may develop.

Cyanosis is usually noted about eight to twelve hours after the onset. The lips and nails are blue and the skin is livid. This picture suggests the diagnosis of early pneumonia.

Petechiae follow the cyanosis, involving the face, trunk and extremities. The lesions appear suddenly, varying in size from small petechiae to larger purpuric macules. They occasionally become confluent, to form dark purple patches the size of an orange. Bush and Bailey<sup>8</sup> reported that their patients had conjunctival hemorrhage causing "bloody tears."

In twelve to twenty-four hours the patient is extremely toxic and semicomatose. Breathing is shallow and rapid, respiration may be Cheyne-Stokes type at the end. During the initial illness, the pulse is rapid in relation to the hyperpyrexia and later becomes feeble and thready. The blood pressure is usually low. Neurologic findings are not consistent. Headache is usually severe. Cervical rigidity may or may not be present. Reflexes usually are unchanged.

Netter and Salanier<sup>10</sup> first found meningococci in the smears from purpuric lesions. This

10 Netter, A, and Salanier, M. Présence des méningocoques dans les éléments purpuriques de l'infection méningococcique, *Compt rend Soc de biol* 29:670-673, 1916.

was corroborated by McLean and Caffey,<sup>11</sup> who also found meningococci by direct smear in the purpuric lesions of 83 per cent of 18 cases of meningococcemia. MacLagan and Cooke<sup>4</sup> in 1916 were the first to classify the meningococcus with the syndrome. Sacks,<sup>7</sup> in reviewing the literature, stated that of 21 cases occurring between 1916 and 1937, in only 60 per cent was the meningococcus demonstrated.

The disease is extremely severe. At times leukocytosis with 8,000 to 90,000 white blood cells is seen. Bamatter<sup>12</sup> noted a shift to the left in the cells of the myelogenous series. The polymorphonuclear count may be as high as 95 per cent.

#### PATHOLOGY

Sacks stated that the most outstanding pathologic finding is a severe bilateral adrenal hemorrhage. This was seen in 95 per cent of the cases. Aegerter, in his review of the literature, found 52 cases in which there was bilateral adrenal hemorrhage. Microscopically destruction of the medullary tissue is seen, and many areas are replaced by extravasated blood. Several areas show complete obstruction of the three glandular layers. The purpura is probably due to the involvement of the capillaries and arterioles by the causative organism or its toxin. Other pathologic findings are similar to those of any severe acute infection.

#### PROGNOSIS AND THERAPY

Aegerter stated that the disease had been fatal in all cases described to 1936. Recently patients of Carey,<sup>13</sup> Rucks and Hobson<sup>14</sup> and Bush and Bailey have recovered.

The duration of the disease is usually about twenty-four to forty-eight hours. The overwhelming septicemia with its fatal hemorrhage is thought to be the feature of this entity.

The high mortality indicates that treatment is imperative and should be immediate, as a delay

of several hours may be fatal. Aegerter suggests massive doses of cortical extract, epinephrine and intravenously injected dextrose and blood transfusions. Bush and Bailey added sulfadiazine intravenously and injection of desoxycorticosterone. One should combat anoxemia (when the patient is cyanotic) by the use of an oxygen tent.

#### REPORT OF CASE

*History*—A 37 year old Filipino was seen on July 2, 1944, with a history of mild malaise, fever and chills and a suggestive purpuric rash on the trunk, arms and legs. The rash had been present only a few hours. His past history was irrelevant. A tentative diagnosis of erythema multiforme was made.

The patient was admitted to Queen's Hospital twenty-four hours later, complaining of a dull headache, slight nausea and occasional vomiting, with abdominal pain and muscular tenderness. He was conscious and partly aware of his surroundings.

*Examination*—Examination showed a well developed man apathetic in appearance. The temperature was 99 F, pulse rate 98, respiration 28 and blood pressure 100 systolic and 70 diastolic. The pupils were equal and responded to light and in accommodation. The ocular fundi showed no papilledema. The nose and throat were slightly congested. The chest was clear. The heart was normal in size, rhythm, rate and sound. Deep and superficial reflexes were normal. The muscles of the extremities were tender on palpation. The abdomen was tense, tender and bloated. There was a diffuse macular purpuric rash with lesions varying in size from a few millimeters to that of a silver dollar. There were no lesions on the palms and soles.

Urinalyses gave normal results. Laboratory tests showed hemoglobin 16 Gm, red blood cells 5,360,000, white blood cells 29,500, polymorphonuclears 94, lymphocytes 4, eosinophils 2, bleeding time three minutes and thirty seconds, platelets 375,690 and sedimentation rate 10 millimeters per hour. A blood culture was taken at this time.

*Treatment and Course*—In a few hours the patient's condition became critical, as evidenced by cyanosis, delirium and a severe chill. The rectal temperature was 107 F, the pulse weak and thready, with a rate of 144 a minute. The blood pressure was 90 systolic and 60 diastolic. Respiration became labored. The patient was incontinent of stools and urine. The purpura became severe, with conjunctival hemorrhages resembling hemorrhagic tears.

Dr. A. S. Hartwell, an internist, was called in consultation and a diagnosis of acute septicemia, cause unknown, was submitted. This was substantiated by a hemogram by Dr. Kandel Hamre (hematologist).

The case puzzled us, as the sequence of events was not clear. That day the diagnosis of Waterhouse-Friderichsen syndrome was suggested by Dr. Stewart Doolittle in an informal discussion. The credit for saving this man's life can be given to Dr. Doolittle, as immediately adrenal cortex extract was given intramuscularly and 5 Gm of sulfadiazine intravenously and 1 Gm of sulfadiazine by mouth every four hours. Plasma was injected intravenously plus 5 per cent dextrose in

11 McLean, S., and Caffey, J. Endemic Purpuric meningococcus Bacteremia in Early Life, *Am J Dis Child* **42** 1053-1074 (Nov.) 1931.

12 Bamatter, F. Fulminante Meningokokkensepsis. *Zur Aetiologie des Syndroms von Waterhouse-Friderichsen*, *Jahrb f Kinderh* **142** 129-162, 1934.

13 Carey, T. N. Adrenal Hemorrhage with Purpura and Septicemia (Waterhouse-Friderichsen Syndrome) with Recovery. *Case Report*, *Ann Int Med* **13** 1740-1744 (March) 1940.

14 Rucks, W. L., and Hobson, J. J. Purpura Fulminans (Waterhouse-Friderichsen Syndrome). *Report of a Case with Recovery*, *J Pediat* **22** 226-232 (Feb.) 1943.

saline solution. Oxygen therapy was instituted for the cyanosis.

There was a dramatic change in the clinical picture in four hours after the aforementioned therapy was started. The temperature dropped from 106 F to 98 F in eight hours and wavered around 100 and 101.4 F for several days. The pulse and respiration rates dropped to normal. The patient's color improved, and he appeared more alert. The purpura remained about the same for four or five days and gradually faded, leaving pigmentation. The only setback appeared three days later, with severe seizures of coughing. The diagnosis of early bronchial pneumonia was thought to be due to retained secretion and to the known hemoptysis. This rapidly cleared in a few days. Administration of adrenal cortex was stopped in five days, and sulfadiazine was discontinued on the sixth day of the illness.

Results of urinalysis remained within normal limits. Examination revealed red blood cells 4,600,000, hemoglobin 14.6 Gm, white blood cells 13,200, polymorphonuclears 69, lymphocytes 16, eosinophils 13 and monocytes 2. The sulfadiazine level reached 17.5, the blood culture was sterile, and the spinal fluid was sterile after ten days. There was no occult blood in the stool.

The remainder of the convalescence was uneventful, and the patient returned to work in four weeks.

#### COMMENT

The Waterhouse-Friderichsen syndrome is a rarity in dermatologic literature but has been described in recent journals on internal medicine. Because of the early purpuric rash the dermatologist may be the first to see a case of this disease or may be called in consultation. The entity is now being recognized, and therapy must be started as soon as the diagnosis is established. In an epidemic of meningitis it is possible that a certain number of cases will be found which will have the clinical features of the Waterhouse-Friderichsen syndrome.

The adrenal hemorrhages seen in these fulminating septicemias have suggested that the cause of death is acute failure of the adrenal cortex. Hyperthermia, hypotension, vascular collapse, abdominal pain, vomiting, cyanosis and purpura are essential for the diagnosis. Meningococcal infections usually produce the syndrome, but overwhelming sepsis due to other organisms may give rise to similar adrenal hemorrhages. Boger states that not all patients who die with a clinical picture of Waterhouse-Friderichsen syndrome present adrenal hemorrhages. Therefore Boger believes that it seems ambiguous to use the term "recovery" in speaking of a cure of Waterhouse-Friderichsen syndrome, since adrenal hemorrhage can only be suggested if the patient survives. He suggests the name "fulminating meningococcemia" in preference to Waterhouse-Friderichsen disease and that the latter should be restricted to pathologic discussions.

Dr. H. M. Izumi,<sup>15</sup> of the island of Maui, reports 2 cases of Waterhouse-Friderichsen syndrome occurring in Filipino plantation workers. The meningococcus was isolated by blood culture. Both patients survived because of early administration of penicillin intramuscularly and sulfadiazine intravenously. An interesting feature is the fact that both Filipinos were employed in the same gang and apparently were infected by one another or by another carrier.

Recently Cosgriff<sup>16</sup> found a decrease in the serum sodium and an increase in the nonprotein nitrogen, compatible with adrenal cortical insufficiency.

Acute severe septicemia initiates the disease; consequently rapid and adequate chemotherapy must be instituted. Sulfadiazine is the drug of choice and should be administered intravenously and subcutaneously and even by the oral route. Penicillin will probably be used. Adrenal cortex extract is helpful in combating the possible adrenal insufficiency. Continuous intravenous injection of fluid should be employed for circulatory collapse.

The increase in reports of cases of the Waterhouse-Friderichsen syndrome indicates a mild epidemic in certain areas. The syndrome is of interest to the dermatologist as well as to the internist. This common interest is also observed in acute disseminated lupus erythematosus and many other syndromes.

#### SUMMARY AND CONCLUSIONS

A case of Waterhouse-Friderichsen syndrome with recovery is reported.

The characteristic clinical history usually states that the patient was well until the sudden attack of the disease. The first reaction may be malaise, restlessness, chills, headaches or vomiting. Abdominal pain is of frequent occurrence. Hyperpyrexia may be severe. The patient becomes lethargic and stuporous and may have convulsions.

Cyanosis is usually noted eight to twelve hours after the onset. The skin is livid, and the lips and nails are blue. Petechiae appear and vary from small to larger purpuric macules.

In a few hours the patient is extremely toxic and semicomatose. The clinical picture is compatible with severe vascular collapse.

15 Izumi, H. M. Personal communication to the author.

16 Cosgriff, S. W. The Waterhouse-Friderichsen Syndrome. Observation on Associated Adrenal Insufficiency and Report of Four Cases, *Ann Int Med* 21: 187-193 (Aug) 1944.



The meningococcus has been classified with the syndrome in many cases. Other organisms have been isolated in recent cases. It is not unusual to find normal blood in spinal fluid cultures.

The outstanding pathologic finding is a severe bilateral adrenal hemorrhage. There are destruction of medullary tissue and areas replaced by extravasated blood.

The high mortality indicates that treatment must be immediate. It is suggested that massive doses of adrenal cortex extract be given, also

epinephrine, intravenously injected dextrose, blood transfusions, sulfadiazine intravenously and desoxycorticosterone. Anoxemia is to be treated by use of an oxygen tent or similar therapy. Penicillin probably will be added to the list of therapeutic possibilities.

This syndrome will be seen by the dermatologist, probably because of the purpura. The recognition of this disease entity within the first twenty-four to forty-eight hours is imperative, as the suddenness of death necessitates early diagnosis and therapy.

# COLLOIDOCLASTIC SHOCK FOLLOWING INJECTION OF OXOPHENARSINE HYDROCHLORIDE (MAPHARSEN)

## REPORT OF A CASE

ARTHUR L SHAPIRO, M D

CHICAGO

The following case is reported because of the rarity of colloidoclastic shock and nitritoid reactions after the injection of oxophenarsine hydrochloride (mapharsen)

## REPORT OF CASE

G S, a white man aged 39, gave a history of having blastomycosis, apparently limited to the skin, of four years' duration. On examination in the University of Chicago Clinics on Dec 15, 1944, he had presented numerous ulcerated infiltrates, measuring from 1 to 4 cm in diameter, distributed over the back, thighs, left leg and right arm. Budding blastomycetes were found in direct smears of the pus expressed from these lesions.

Biopsy section disclosed conditions compatible with a diagnosis of blastomycosis, but no micro-organisms could be demonstrated in the tissue.

The patient's general physical condition was good. Fluoroscopic examination of the chest showed no pulmonary involvement. Wassermann and Kahn tests elicited negative reactions. The white blood cell count was 8,800, and the hemoglobin content was 14 Gm. The urine was normal.

Since there was a history of sensitivity to iodides, it was decided to try arsenical therapy, as recommended by Stokes,<sup>1</sup> in addition to local roentgen ray treatment. The patient had never had arsenicals before. He was given 0.02 Gm of oxophenarsine hydrochloride intravenously without any reaction on Dec 23, 1944. On December 30 he was given the second injection of oxophenarsine hydrochloride, 0.03 Gm by the usual intravenous technic. After this second injection he complained of pain along the entire arm, this was interpreted as venous cramping. However, he felt well enough to get off the table. Almost immediately he complained of feeling ill and became ashen gray, about one minute later he collapsed and stopped breathing. The eyes remained open, staring sightlessly. The skin was clammy, and perspiration could be seen on the face.

Artificial respiration was administered immediately. After about a minute the patient gasped. The gasping was repeated several times but with long intervening apneic periods. Finally, he began to breathe irregularly. During an interruption of artificial respiration, about three minutes after the onset of the reaction, 0.5 cc of solution of epinephrine hydrochloride (1:1,000) was

From the Section of Dermatology, Department of Medicine, University of Chicago.

1 Stokes, J H, and others. *Fundamentals of Medical Dermatology*, Philadelphia, University of Pennsylvania Department of Dermatology Book Fund, 1942, p 350. Stokes, J H, Beerman, H, and Ingraham, N R. *Modern Clinical Syphilology*, Philadelphia, W B Saunders Company, 1944, pp 151 and 409-411.

administered hypodermically. The pulse was thready but soon became full and slower, although it had a bigeminal character at first. The patient apparently recovered completely within one-half hour, but two days later he experienced severe pain in the back and in the right testicle and suffered from a severe headache which lasted for three days. He was last seen in this clinic on Jan. 6, 1945, one week after the shock reaction, feeling weak and having a slight amount of testicular pain. Subsequently, he was treated by his family physician with local heat, sodium thiosulfate, pyridium (phenylazo-alpha-diaminopyridine monohydrochloride) and sedation because of severe testicular pain which lasted about one week, and after that he was treated for severe pain over the region of the kidneys. Urologic examination, including cystoscopy, failed to reveal renal involvement. On February 3, the patient was doing well, according to a report from his physician.

## COMMENT

Stokes, in his textbooks,<sup>1</sup> differentiates sharply between a nitritoid reaction and colloidoclastic shock. In the typical nitritoid crisis the patient is primarily "flushed, hyperactive, coughing, choking and with a bounding pulse," while in colloidoclastic shock he is "pale, pulseless and collapsed." However, according to the same author, in the final stage of the nitritoid vascular reaction the patient becomes unconscious, and he may also become pulseless and collapse. This last phase of the nitritoid crisis is rather similar to the syndrome of colloidoclastic shock. My patient had the symptoms of colloidoclastic shock and not those of the first stages of a nitritoid reaction. It is possible, however, that because of the severity of his reaction the final stage of nitritoid crisis was the only one observed.

In any case, a review of the literature reveals that both a nitritoid reaction and colloidoclastic shock following injection of oxophenarsine hydrochloride are rare. Levin and Keddie<sup>2</sup> reviewed the literature from 1935 to 1941, and although they reported the case of a patient displaying "shock, pallor, weakness, nausea and vomiting," they stated that no true nitritoid reaction was described. They reported, however,

2 Levin, E A, and Keddie, F. *Toxic Effects Following the Use of Mapharsen*, J A M A. **118**:368-372 (Jan 31) 1942.

42 cases in which there were severe repeated nitritoid crises following the injection of arsphenamines and stated that these patients on the other hand tolerated oxophenarsine hydrochloride without any reaction resembling a nitritoid crisis

Carter, Chambers and Anderson,<sup>3</sup> in a statistical review of all cases in the Navy and Marine Corps, Veterans Administration and native population of insular possessions in which oxophenarsine hydrochloride was used from 1935 to 1942 inclusive, reported only 1 severe vasomotor reaction (followed by death) from a total of 397,680 doses. However, resulting from 1,364,814 injections of neoarsphenamine, administered from 1925 to 1942, there were 63 severe vasomotor reactions, including 6 deaths, this is a ratio of 1 to 21,664. In 1942, resulting from 109,095 injections of oxophenarsine hydrochloride there were 2 mild vasomotor reactions but the described symptoms were not typical of nitritoid crisis or colloidoclastic shock.

3 Carter, T J, Chambers, W M, and Anderson, L T. Toxic Effects of Arsenical Compounds, U S Nav M Bull 42 229-241 (Jan) 1944

Stokes, Beerman and Ingraham,<sup>4</sup> in a review of the literature on reactions to arsenicals in the treatment of syphilis, made no mention of nitritoid reaction following administration of oxophenarsine hydrochloride. Simon and Iglauer<sup>5</sup> described their patient's reaction to the fifth injection of oxophenarsine hydrochloride as "faintness almost to the point of syncope." Cole and Palmer<sup>6</sup> recorded 4 instances of vascular crisis or reaction resembling nitritoid reaction but stated that the notes in the charts of these patients were insufficient for them to draw a definite conclusion. No other instances of nitritoid reaction or colloidoclastic shock following injection of oxophenarsine hydrochloride were found in the literature available to me.

4 Stokes, J H, Beerman, H, and Ingraham, N R. The Trivalent Arsenicals in Syphilis, Am J M Sc 202 606-624 (Oct) 1941

5 Simon, S R, and Iglauer, A. Death Following Mapharsen Therapy, Am J Syph, Gonorr & Ven Dis 23 612-616 (Sept) 1939

6 Cole, N H, and Palmer, R B. Mapharsen in the Treatment of Syphilis, Arch Dermat & Syph 36 561-580 (Sept) 1937

# CARBARSONE IN THE TREATMENT OF PEMPHIGUS

## A PRELIMINARY REPORT

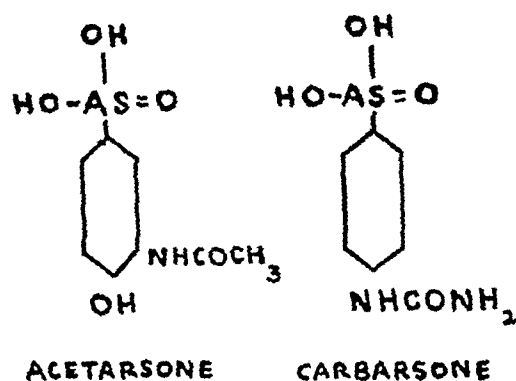
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Arsenic, of all the drugs used in the treatment of pemphigus, has withstood the test of time. Although it has been condemned by a few investigators as being of no benefit or even harmful, in the majority of cases of patients reported improved or cured arsenic is the medicament most frequently mentioned. It has been employed as solution of potassium arsenite U S P, sodium and iron cacodylate, old arsphenamine, neoarsphenamine, tryparsamide and others. Just why arsenic should be beneficial in treatment of pemphigus is not known. It may be parasitocidal, for it is an interesting observation that many of the preparations credited with "cures" have been protozoal poisons, such as quinine, antimony and potassium tartarate, Geimann and compounds such as tryparsamide and acetarsone. It seems more probable, however, that arsenic is merely a tonic acting on the nerves, gastrointestinal tract, reticuloendothelial cells, endocrine glands and skin. It is conceivable that some preparations may be more curative and less toxic than others, but only experimentation and knowledge of the cause of the disease will determine which is the best. Recently acetarsone has been the subject of keen interest because of favorable reports in the literature.

The first report on the use of acetarsone was made by M. Oppenheim<sup>1</sup> before the Viennese Dermatological Society in November 1927. In 1929 Kromayer,<sup>2</sup> in the *Deutsche medizinische Wochenschrift*, wrote of having obtained benefit in 6 cases of pemphigus, 2 of severe pemphigus, by the use of *spirozid* (acetarsone). He concluded that by treatment with acetarsone pemphigus, if not cured, loses its acute character and assumes a chronic inflammatory type. In 1943 Oppenheim and Cohen<sup>3</sup> reported good

results from the use of the drug. Acetarsone is no. 594 in Ehrlich's series and is 3-aminoacetyl-4-hydroxyphenyl arsonic acid. It has been used in the prophylaxis and treatment of syphilis but has not attained extensive popularity because it is unreliable and toxic. It now finds its principal use in the treatment of congenital syphilis and amebic dysentery. However, the reports on its use for patients with pemphigus are encouraging (it is probably the best drug so far suggested), nevertheless, its toxicity would prompt caution in its use against a chronic disease for which treatment must be prolonged. Arsenical poisoning is said to occur in approximately 1 of 6 patients (when acetarsone is used against syphilis). A therapeutic



Structural formulas of acetarsone and carbarsone

axiom is, "First, do no harm." Patients ill of pemphigus are already depressed and toxic from disease.

An ideal arsenical to be used against a chronic disease should be well borne of low toxicity, suitable for oral administration over a considerable time, of high therapeutic efficiency and yet of comparatively low price. For pemphigus, why not seek a preparation resembling acetarsone, which for some reason has proved to be effective?

It occurred to me that carbarsone, also a pentavalent arsenical (28.5 per cent arsenic), with a structural formula resembling that of acetarsone but much less toxic, was worthy of

<sup>3</sup> Oppenheim, M., and Cohen, D. Acetarsone in the Treatment of Pemphigus, *Arch. Dermat. & Syph.* 47:40 (Jan) 1943.

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<sup>1</sup> Oppenheim, M. Pemphigus chronicus serpiginosus. *Zentr. f. Haut- u. Geschlechtskr.* 26:350, 1927.

<sup>2</sup> Kromayer. Sechs durch Spirozid geheilte (?) Pemphiguskfälle, *Deutsche med. Wochenschr.* 55:229, 1929.

trial Carbarsone (paracarbamidophenyl arsonic acid) was studied and introduced as an amebicide by Anderson and Reed<sup>4</sup> in 1931. It has also been used in the treatment of *Trichomonas vaginalis* infections. It is of low toxicity (one eighth that of acetarsone), is of high therapeutic efficiency (twelve times that of acetarsone) and is relatively cheap. Carbarsone has recently been admitted to the "Pharmacopeia of the United States" and is a pentavalent organic arsenical, insoluble in water but readily absorbed from the gastrointestinal tract and slowly excreted. It is contraindicated for persons with hepatic or renal disease, and, as with other pentavalent arsenicals, changes in vision should be watched for, though to my knowledge serious changes have not been reported. Local edemas, diarrhea, nausea, vomiting, abdominal pains and mild cutaneous eruptions have been observed. According to Goodman and Gilman,<sup>5</sup> carbarsone is one of the most innocuous of organic arsenicals, and deaths from its use have been extremely rare.

In April 1944, the use of carbarsone in the treatment of pemphigus was begun in Bellevue Hospital in the dermatologic service of Dr. Frank C. Combes. With the cautions and contraindications mentioned in mind and in order to avoid a cumulative effect, a scheme of intermittent dosage was adopted as follows: 1 or 2 (0.25 Gm.) capsules for three days (one-half hour before breakfast), followed by a rest for three days. Improvement with this schedule was noted after three or four weeks. In view of the slowness in improvement, a more intensive dosage could be tried in the beginning. A suggested schedule is 1 capsule (0.25 Gm.) twice a day for ten days, followed by a rest for ten days. This, in turn, is followed by the three day dosage and three day rest plan.

Since carbarsone is an arsenical and may prove to be hepatotoxic, a test of hepatic function

should precede treatment and a blood count and urinalysis made once a week. As a further precaution, the visual fields may be examined and checked, though so far "despite the paraposition of the amido group serious optic damage is almost unknown."<sup>5</sup> Laboratory work, such as determinations of chloride level, sedimentation rate and albumin-globulin ratio and Pels-Macht tests, is interesting to help confirm the diagnosis and to follow the course of the disease as well as to afford a criterion for recovery.

The good results in this brief series of cases should not blind one to the fact that pemphigus is a most serious disease and that the third attack is usually fatal, in spite of encouraging remissions. A nourishing diet, vitamins, transfusions of blood and plasma, and above all the good nursing care that patients receive in this hospital are to be weighed and given the credit they deserve in the improvement in these cases. Routinely, patients received daily 50,000 U. S. P. units of vitamin A, 1 Gm. of brewers' yeast, 2 mg. of riboflavin, 50 mg. of ascorbic acid and 50 mg. of nicotonic acid.

#### COMMENT

Under the plan described, use of carbarsone has been continued to date without intermission, except in a single case in which edema was noticed localized to the face and hands which disappeared with temporary discontinuance of the drug. Of 17 patients with pemphigus, 5 died, 6 have been discharged with the disease arrested, 5 are under treatment greatly improved and 1 was transferred to another service in an improved condition. Of those who died, some were moribund and all were in poor condition on admission. Among those discharged and those still under treatment are many who were seriously ill, 1 who had pemphigus vegetans, others who had widespread bullae and 1 who had deep bedsores.

#### CONCLUSION

Carbarsone is suggested for the treatment of pemphigus.

147 Avenue B

<sup>4</sup> Anderson, H. H., and Reed, A. C. Amebiasis. Comments on Various Amebicides, Report of Case, *California & West Med* **35**: 439, 1931.

<sup>5</sup> Goodman, L., and Gilman, A. Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1940.

## Clinical Notes

### FEVER AND STERILE ABSCESS FORMATION ACCOMPANYING TREATMENT OF SYPHILIS WITH PENICILLIN

M EDWARD GOEBEL, M D, AND ARTHUR W GRACE, M D, BROOKLYN

Mahoney<sup>1</sup> and Stokes,<sup>2</sup> with their collaborators, have reported the occurrence of fever and abscess formation in persons undergoing treatment for syphilis with penicillin. The case presented here includes features not mentioned by those authors.

#### REPORT OF A CASE

J M, a white man aged 40, when first seen, on Jan 15, 1945, had a nodular ulcerative syphilid on the extensor aspect of the right forearm which had been present for two years. The physical condition was good, and a general examination revealed no other abnormalities. The Wassermann reaction of the blood was 4 plus, and complete fixation of the complement occurred with 0.2 cc of cerebrospinal fluid.

Therapy was commenced with oxophenarsine hydrochloride (mapharsen) and a bismuth preparation

back. Within two days this reaction had subsided, and therapy with oxophenarsine and bismuth was resumed, only to be abandoned entirely after a single injection of each drug had produced the same untoward effects. On this occasion the reaction was accompanied with epistaxis and was sufficiently severe to confine the patient to bed for four days.

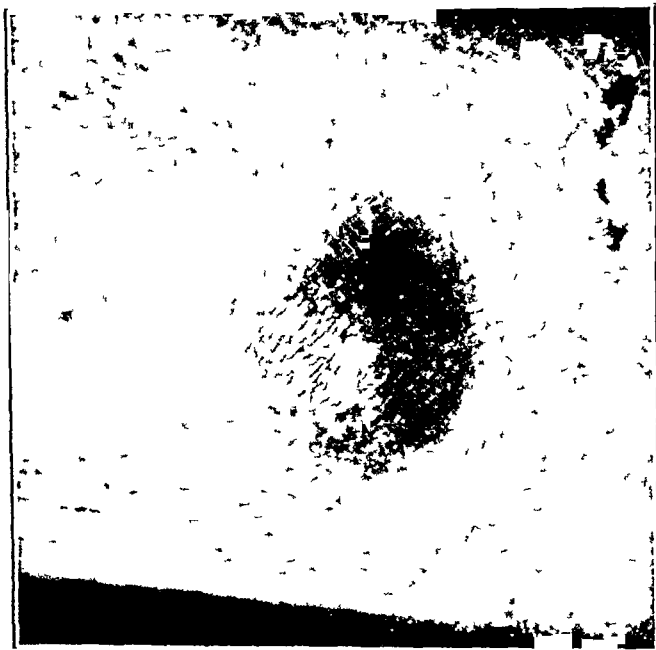
On February 20, ten days after the subsidence of the reaction, treatment with penicillin was commenced, 25,000 oxford units being injected intramuscularly at three hour intervals. After twenty doses had been given, the patient's temperature rose to 103.2 F. in eight hours, and there was decided congestion and some edema of the soft palate, uvula, fauces and pharynx. Also, indurated, erythematous, edematous, painful areas, 4 to 6 inches (10 to 15 cm) in diameter, appeared in the buttocks at the sites of injection of penicillin. Similar areas appeared on the chest and back at uninoculated sites, and one was found over the great trochanter of the left femur, where a subcutaneous injection of dihydromorphine hydrochloride had been given. Fluctuation appeared in two of the indurated areas, and 3 cc of thick, inodorous pus mixed with blood was aspirated from one.

No micro-organisms were found on direct smear or on aerobic or anaerobic culture of the pus, and dark field examination did not reveal the presence of spirochetes. A white cell count performed on February 25 showed 29,600 leukocytes per cubic millimeter of blood, of which 93 per cent were of the polymorphonuclear series. A culture of the blood at the height of the febrile reaction was sterile, and cultures of material from the edematous throat tissue showed *Micrococcus catarrhalis* together with hemolytic and nonhemolytic streptococci. A culture of the dihydromorphine hydrochloride used for subcutaneous injection was bacteriologically sterile, and other patients inoculated with the same preparation and penicillin solutions as were used on J M did not show any local or general reaction.

The appearance of the nodular ulcerative syphilid on the forearm was unchanged throughout the entire period of observation. It became necessary, after 1,000,000 units of penicillin had been given, to discontinue penicillin treatment, on February 25, owing to the development of incessant vomiting and slight delirium. Fever persisted until March 4, the temperature reaching a maximum of 104.6 F on February 24 and remaining above 102 F through February 28. Both pulse and respiration rates rose and fell with the temperature. All symptoms except slight soreness of the throat had disappeared when the patient was last seen, on March 7, 1945.

#### COMMENT

In view of the fact that nonsyphilitic persons were treated without reaction with the same solution of penicillin as was used on a person whose only detectable disease was syphilis, it is reasonable to assume



Bacteriologically sterile abscess over the great trochanter of the femur

After four injections of the former and two of the latter had been given in ten days, treatment was suspended, owing to the development of chills, fever, anorexia, vomiting and pain in the lower part of the

From the Long Island College Hospital and the Department of Dermatology and Syphilology, Long Island College of Medicine

<sup>1</sup> Mahoney, J F, Arnold, R C, Sterner, B L, Harris, A D and Zwally, M R. Penicillin Treatment of Early Syphilis, J A M A 126:63 (Sept 9) 1944

<sup>2</sup> Stokes, J H, Sternberg, T H, Schwartz, V H, Mahoney, J F, Moore, J E, and Wood, V B. The Action of Penicillin in Late Syphilis, A M A 126:73 (Sept 9) 1944

that the reaction sustained by that patient was due to the action of penicillin on *Treponema pallidum*. Consideration of the nature of the action can only be speculative and must be founded on the effect on the tissues of the products of destruction of the spirochete, such effect being brought about either directly, by a primary irritant, or indirectly, through an antigen-

antibody reaction. The absence of reaction at the site of the gummatous lesions on the forearm can be interpreted on the basis of an assumption that the development of the lesion, two years prior to therapy with penicillin, had exhausted some or all of the materials essential to reaction with spirochetal products at that site.

## ERYSIPELOID TREATED SUCCESSFULLY WITH INJECTIONS OF PENICILLIN

### Report of a Case

MAURICE J. COSTELLO, M.D., NEW YORK

P. W., a white woman aged 66, was examined on July 10, 1945, because she complained of a papular urticarial eruption on the limbs which had been present for about five days. At this time she called attention to an eruption confined to the third finger of her right hand. She stated that on July 7 she cleaned a perch, and one of the sharp scales became embedded in her finger. The finger presented a mottled red appearance. It was swollen and shiny and painful to pressure. There were pain and stiffness when the finger was flexed. The portal of entry of the infection was at about the middle of the medial aspect of the finger, where there was a whitish spicule embedded in the skin. The patient's temperature was 100.2 F. She was advised to apply wet compresses and to return to the office in one week.

On July 17, 1945, the condition had become worse, and it was decided to hospitalize the patient. She was admitted to St. Clare's hospital, where she was given 40,000 units of penicillin by intramuscular injection, at 8:00 and 11:00 a.m. and 2:00, 5:00 and 8:00 p.m. daily, until she had received 1,800,000 units over a period of nine days. On July 27 there was complete involution of the eruption with disappearance of the swelling and pain, and the skin began to exfoliate. On July 30 there was slight residual redness at the dorsal surface of the last phalanx, but the patient was apparently cured. It is believed that the response could have been even more rapid if the patient had received eight similar injections daily, rather than five, but the patient's age and infirmity had to be considered.



## Correspondence

### SEMBLANCE OF ELASTIC TISSUE TO MYCELIUM IN POTASSIUM HYDROXIDE PREPARATIONS

*To the Editor* —I have read with interest a clinical note entitled, "Semblance of Elastic Tissue to Mycelium in Potassium Hydroxide Preparations," by Walter S. Green and Maurice C. Shepard in the August issue of the *ARCHIVS OF DERMATOLOGY AND SYPHILIOLOGY*. I should like to call attention to the work of two American authors, Isaac R. Pels and S. Bayne-Jones of Baltimore, who published in 1923 an article on exactly the same subject (Elastic Tissue Simulating Mycelial Filaments in Skin Scrapings, *ARCH DERMAT & SYPH* 8 37 [July] 1923). These authors stated that elastic tissue fibers in scrapings from lesions of the skin may so closely resemble the mycelial filaments of fungi as to lead to an error in diagnosis and the consequent use of inappropriate treatment. Their specimens, taken from granulomatous lesions and examined in potassium hydroxide, contained filaments which were mistaken for fungous mycelium by a number of competent observers. The filaments were delicate, long and hyaline, from 1.5 to 5 microns in diameter, with irregular width and apparently doubly contoured edges. The internal structure was glassy and almost free from granules. Some of the fibrils branched irregularly, others contained transverse striations which suggested septums. The ends of the fibrils were either blunt or tapering or were split longitudinally into a few smaller fibrils. The ends were often spirally curled. Along the sides of some of the fibrils were small prominences suggesting budding. All attempts to culture a fungus from the material containing these fibrils failed. Their peculiarities—the glassy nature and the curling and splitting ends—suggested the elastic tissue origin, which was finally proved by staining with Weigert's elastic tissue stain. The fibrils appeared dark purple or almost black with homogeneous structure.

C. Brulius and A. Alexander (in Jadassohn, J. "Handbuch der Haut- und Geschlechtskrankheiten," Berlin, Julius Springer, 1928, vol. 11, p. 89) mentioned the elastic fibers as the number one cause of mistakes in examination of skin scrapings for fungi. They are found when the material consists not of superficial scrapings but of bits of deeper tissues in cases of granulomatous or ulcerated lesions. According to these authors, the elastic fibers never divide dichotomously and therefore can easily be distinguished from fungous filaments, which show such a division. It seems to me, however, that this remark will be of little help, because the true fungous filaments often show an irregular division. I believe that the most important diagnostic feature of fungous filaments will be their distinct septation and their tendency to break into chains of spores.

The technic of taking material for examination has much to do with the presence of elastic fibers in the preparation. As they are a normal constituent part of the corium, it is natural to obtain them if bits of tissue are taken from the deep inflammatory or ulcerated lesions extending into the corium. The common fungous diseases of the skin are superficial. The fungi are

present only in the cornified layers of the epidermis. There is no need for penetrating into the corium with instruments. This, however, is difficult to avoid if a sharp scalpel is used to take shavings of skin. By using a not very sharp curet and taking scrapings rather than shavings, one can confine the action to the epidermis and thus avoid the presence of elastic fibers in the preparations.

It seems to me that these fibers cannot be called an "artefact." This term can properly be used in relation to structures artificially produced by laboratory procedures, for instance, air bubbles, oil droplets, granules of cellular detritus, crystals of potassium hydroxide, etc. The elastic fibers are a normal part of the skin and are no more an artefact than are epidermal cells or leukocytes.

E. MUSKATBLIT, M.D., New York

55 West Forty-Second Street

*To the Editor* —In the August issue of the *ARCHIVES* (52 115, 1945) under the title of "Semblance of Elastic Tissue to Mycelium in Potassium Hydroxide Preparations," Drs. W. S. Green and M. C. Shepard call attention to a condition which was described some time ago by Dr. S. Bayne-Jones and me (Elastic Tissue Simulating Mycelial Filaments in Skin Scrapings, *ARCH DERMAT & SYPH* 8 37-43 [July] 1923). Our article was based on a study of 2 cases of granulomas of undetermined origin.

In the light of these publications it should be stated that open or eroded areas examined for fungi should be suspected of revealing elastic tissue which may simulate mycelial filaments. It is of course timely to reiterate this concept in view of the importance of establishing a diagnosis.

We could find no mention of this experience in the literature preceding our publication.

ISAAC R. PELS, M.D., Baltimore

### DEMONSTRATION OF EFFECT OF NUTRITION ON THE SKIN

*To the Editor* —Because there are differences of opinion with regard to the effect of nutrition on the skin, the following record of prolonged observation is offered for your consideration.

About 1890 the Lanette, Ala., cotton mills were built on the farm on which I was born and a cottonseed oil press operated nearby. Housewives gathered around a demonstration of the use of this oil in cooking. In 1896, as a freshman who preferred books to meat, I went on a Hindhede diet (chiefly bread and milk) for three months. My skin became rough and irritable but cleared up after three months of eating fat meat and drinking oil. In 1912 I drank 1 ounce (28 cc) of cottonseed oil every day for six months, with similar results.

In 1918, while I was serving with the Nutrition Division, United States Army, an exudative eczema developed that interfered with military duty. Allergy tests elicited negative reactions. Fat meat relieved the

eczema, whereas dairy products did not, in fact, sometimes a meal with much cream made it worse. Since the high fat diets were low in carbohydrate, I tried a diabetic diet for a year. This relieved the eczema but lowered my sugar tolerance, and when I returned to a normal diet furunculosis developed, of which I have had repeated attacks to the present time. The lowered sugar tolerance was not accompanied with glycosuria, even after I had taken 250 Gm of glucose, but there was a delay in return of the blood sugar to normal. With insulin, I could reduce my blood sugar to 37 mg per hundred cubic centimeters without losing consciousness.

In 1930, after reading the papers of Urbach and collaborators, I became interested in the sugar and water contents of the skin and made determinations on the skin of rats fed various diets. Urbach now calls the condition "skin diabetes." From a dietary standpoint, however, there seems to be a distinction between the diet relieving eczema and that relieving furunculosis.

Furunculosis is relieved by reducing the rapidly absorbed carbohydrates (replacing them with any fat). But, as Burr and Burr first showed with rats and Arild Hansen with children, eczema is relieved only by linolic and arachidonic acids.

There was always a return of eczema on stopping use of the essential fatty acids, and I have purposely let it return at least once every five years. Since 1918 I have drunk 5 gallons (187 liters) each of corn, cottonseed and raw linseed oils and eaten 40 pounds (18 Kg) of lard to control eczema.

In 1932, in a paper in the Tokyo Iz1 Sins1 (no 2907), I attributed the effect of linolic and arachidonic acids to the formation of their choline-glycerophosphate and cholesterol esters, which waterproofed the epidermal cells of the skin. This was based on electrical resistance and chemical studies of the cells and on the fact that eczema (especially the itching) was made worse by the passage of water through the skin due to alternate wetting and drying.

J F McCLENDON,

Lt Col, U S Army Reserve, Nutrition Div  
Hahnemann Medical College, Philadelphia

## Obituaries

KENDAL FROST, M D

1890-1945

Kendal Frost, son of Dr Fred R Frost and Mary Humphreys Green, was born Nov 9, 1890, at Los Angeles. After graduating from a private boys' school, he attended the University of California and obtained a B L degree in 1913 and

the American Forces. Altogether he spent twenty-four months overseas. After the armistice he was with the Belgian Relief Commission.

At the time of his death he was a member of the American Medical Association, American



KENDAL FROST, M D

1890-1945

an M D degree in 1914. He then went to Rush Medical College, and his M D degree was conferred on him in 1916. After that he served an internship at the Presbyterian Hospital in Chicago where he came under the tutelage of Dr Ormsby, of whom he remained a life-long admirer and devoted friend. He was attached for eleven months to the British Expeditionary Forces during World War I, later recalled to

Dermatological Association, American Academy of Dermatology and Syphilology, Inc, Los Angeles Dermatological Society, Los Angeles Academy of Medicine, American College of Physicians, Los Angeles Symposium Society, Los Angeles Museum Patrons Association, California Club, and Theta Delta Chi Fraternity.

Dr Frost was a diligent worker, aside from a yearly vacation his time was largely taken up

with dermatologic activities. He had a busy office practice, occupied the chair of dermatology at the University of Southern California and was in charge of the dermatologic work at the Good Hope Clinic. For many years he was consultant in dermatology to the Santa Fe Coast Lines Hospital and was also on the staff of St. Vincent's Hospital and Hospital of the Good Samaritan. He was one of the founders of the Los Angeles Dermatological Society and remained an active and interested participant in its meetings until his health no longer permitted it. His thinking was always basic and sound, and therefore his participation in the societies' meetings will be sorely missed by his colleagues. He was never the first to accept the new or the last to discard the old. Personal exhibitionism had no part in his program.

Dr. Frost formed a limited number of friendships, and to these friends he remained warmly devoted. His tastes were refined, he was much interested in various musical activities in Los Angeles and was an accomplished pianist. His collection of artistic prints, which he selected himself, are a valuable possession. His social activities were largely carried on in intimate association with his family. Dr. Frost was a native son of California and, while he said little about it, was proud of it. While still comparatively young at the time of his death, he must be looked on as one of the pioneers of modern dermatology in Southern California. He leaves a widow, Mrs. Dorothy Frost, a son, Kendal Jr., and a daughter, Rebecca. He died Sept. 27, 1945, after a long illness.

WILLIAM H. GOECKERMAN, M.D.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

## GENERALIZED VACCINIA IN AN ECZEMATOUS CHILD DEMONSTRATION OF VIRUS AND COMMENT ON "KAPOSI'S VARICELLIFORM ERUPTION" FALLS B HERSHEY and WILLIAM E SMITH, Am J Dis Child 69 33 (Jan) 1945

In this communication from the department of pediatrics and of pathology of the Massachusetts General Hospital, a case is reported of generalized vaccinia occurring in an eczematous child after exposure to a recently vaccinated brother. The vaccine virus was recovered from the cutaneous lesions, and antibodies against this virus were demonstrated in the serum of the patient. The cutaneous lesions of the vaccinia developed almost exclusively in the eczematous areas.

Recently, agents closely resembling herpes simplex virus have been recovered from similar eruptions known as Kaposi's varicelliform eruption or pustulosis varioliformis acuta. Since these eruptions occur in patients with eczema, they were formerly considered to be identical with eczema vaccinatum. However, a considerable number of patients have failed to yield either vaccinia or herpes virus despite appropriate tests. The suggestion is made that this may be due to other viruses localizing in the eczematous areas.

## ACUTE GLOMERULAR NEPHRITIS IN AN INFANT WITH CONGENITAL SYPHILIS JOSEPH YAMPOLSKY and DEWITT F MULLINS JR, Am J Dis Child 69 163 (March) 1945

The authors report a case of acute glomerular nephritis in an infant with congenital syphilis. The observations at autopsy are given. The literature on the causation and diagnosis of hemorrhagic nephritis in the newborn is reviewed. While the authors' patient had congenital syphilis, it is not at all certain that this disease was the cause of the nephritis.

NELSON PAUL ANDERSON, Los Angeles

## SARCOIDOSIS OF BOECK METABOLIC STUDIES OF 3 CASES B M STUART, Am J M Sc 208-717 (Dec) 1944

From extensive studies of 3 patients with sarcoidosis (2 of whom had the uveoparotid syndrome) Stuart found that serum alkaline phosphatase values were elevated while acid phosphatase values were normal. The results of other laboratory procedures merely confirmed the observations of other authors.

LINCH, St Paul

## ABDOMINAL ANEURYSMS VIRGIL SCOTT, Am J Syph, Gonor & Ven Dis 28 682 (Nov) 1944

In 93 patients the presence of abdominal aneurysms was proved by autopsy, by exploratory laparotomy or on the basis of clinical and roentgenologic observations. The cause of the abdominal aneurysms (aorta and branches) in these 93 patients was as follows: syphilis 55 per cent, arteriosclerosis 20 per cent, bacterial 188 per cent, periaortitis nodosa, 1 per cent, tuberculosis, 1 per cent. Multiple abdominal aneurysms were present in 187 per cent of the patients.

The incidence of syphilitic aneurysm was highest in the Negro race (42 per cent) and in the male sex (84 per cent).

The symptomatology of abdominal aneurysm is variable because of the differences in location and size. In the syphilitic group the most significant symptom was pain in the abdomen or back which was present in 84 per cent of the patients. This pain was most severe at night and was relieved by a change of position. A mass exhibiting an expansible pulsation, a palpable thrill and an audible bruit is the most characteristic physical manifestation of abdominal aneurysm. The important roentgenologic changes observed are erosion of the vertebral column resulting from pressure of the aneurysm and the presence of calcium deposits in the wall of the aneurysmal mass. The prognosis is usually grave.

## SYSTEMIC MANIFESTATIONS OF BISMUTH TOXICITY ALBERT HEYMAN, Am J Syph, Gonor & Ven Dis 28 721 (Nov) 1944

Four patients with severe systemic manifestations and renal insufficiency following bismuth therapy are reported on. Two died. The other 2 had severe bismuth melanosis of the large intestine and cervicovaginitis due to bismuth. The role of bismuth in the production of renal insufficiency is discussed, and the relation of previous renal damage to bismuth toxicity is emphasized. Caution is advised in the use of bismuth in treatment of patients with previous renal damage.

## PENICILLIN IN THE TREATMENT OF EARLY SYPHILIS RESISTANT TO ARSENIC AND BISMUTH R A NEL- SON and L DUNCAN, Am J Syph, Gonor & Ven Dis 29 1 (Jan) 1945

Six patients with early syphilis resistant to arsenic-bismuth chemotherapy were treated with penicillin. The cutaneous lesions in all the patients were of the psoriasiform type, and spirochetes could be demonstrated in the material from the lesions of 5 of the 6 patients. Varying dosage schedules were employed, ranging from a total dose of 60,000 to 2,000,000 Oxford units, although on the basis of available information to date the authors would administer 2,400,000 units of penicillin intramuscularly in sixty injections of 40,000 units each, given every three to four hours around the clock.

Penicillin was uniformly successful in destroying surface spirochetes and in healing lesions in all the patients. In some 2,000 patients with early syphilis so far treated with penicillin, no examples of penicillin-resistant syphilis have been as yet encountered.

## INFECTIVITY OF HEMOPHILUS DUCREYI FOR THE RABBIT AND THE DEVELOPMENT OF SKIN HYPERSENSITIVITY R R FEINER and FRANCO MORTARA, Am J Syph, Gonor & Ven Dis 29 71 (Jan) 1945

Lesions were produced in the skin of rabbits by intradermal or multipuncture inoculation of living virulent cultures of *Hemophilus Ducreyi*. Injection by other routes or with heat-killed organisms was without effect. *H. Ducreyi* could be isolated in pure culture from

lesions of rabbits, and from such cultures lesions in new animals could be reproduced and organisms again recovered

A cutaneous hypersensitivity to H. Ducreyi vaccine developed after the production of a cutaneous lesion by intradermal injection of virulent organisms. This hypersensitivity lasted at least three months. No hypersensitivity developed after repeated intradermal injections of the vaccine itself or the injection of living organisms by other routes.

**AN EXPERIMENTAL INVESTIGATION OF THE ETIOLOGY AND IMMUNOLOGY OF GRANULOMA INGUINALE**  
KATHERINE ANDERSON, W. A. DEMONBREUN and E. W. GOODPASTURE, *Am J Syph, Gonorr & Ven Dis* **29** 165 (March) 1945

A micro-organism morphologically identical with the Donovan body of granuloma inguinale and its unencapsulated bacillary forms has been isolated and serially cultivated in the yolk of developing chick embryos. The same micro-organism has been isolated from the lesions of 3 patients with granuloma inguinale. Embryonic yolk in vitro supports the growth of the micro-organism. Washed bacterial bodies stimulate an apparently specific cutaneous reaction in the skin of patients with active granuloma inguinale.

A "capsular" substance which is precipitable from infected embryonic yolk gives an apparently specific precipitation reaction in patient's serum.

**SOBISMINOL MASS IN THE TREATMENT OF SYPHILIS**  
CHARLES W. BARNETT and WILLARD M. MEININGFR, *Am J Syph, Gonorr & Ven Dis* **29** 174 (March) 1945

The authors report their further experience with sobisminol mass in the treatment of syphilis, some five years after their original report in 1939.

Ninety-three patients with early syphilis were treated with sobisminol mass in combination with neoarsphenamine or oxophenarsine hydrochloride. Fifteen patients showed clinical or serologic relapses, an incidence of 16 per cent. The high incidence of relapse was attributed to the type and the irregularity of treatment and the administration of sobisminol mass before use of the arsenicals was started.

In patients with late syphilis sobisminol mass produced a rapid involution of gummatous lesions, and a number of patients with advanced cardiovascular involvement and neurosyphilis were improved symptomatically. The toxicity of the drug is low, but about one third of the patients taking it experienced mild gastrointestinal disturbances. Indications for the use of sobisminol mass are discussed and its superiority to other substances used in antisyphilitic therapy under certain circumstances is pointed out.

**THE CHEMOTHERAPY OF SYPHILIS** JOSEPH E. MOORE, *Am J Syph, Gonorr & Ven Dis* **29** 185 (March) 1945

This is an excellent article which reviews the chemotherapy of syphilis from the first appearance of the disease in Europe, in 1493, until October 1944. The last half of the article is devoted to the use of penicillin in treatment of syphilis, but since the picture regarding penicillin is changing so rapidly, details regarding its use are omitted from this abstract, except the statement that penicillin is a new and powerful addition to syphilotherapy.

REUTER, Milwaukee

**SYPHILIS: REVIEW OF THE RECENT LITERATURE** E. GURNEY CLARK, JOSEPH EARLE MOORE, CHARLES F. MOHR, VIRGIL SCOTT and RICHARD D. HAHN, *Arch Int Med* **74** 390 (Nov) 1944

Mohr and his associates have again provided an extensive, thorough and critical review of literature pertinent to syphilis. The present review covers the period from July 1943 to July 1944 and is divided into sections relating to various laboratory, public health, therapeutic and clinical phases of the disease.

**SPOROTRICHOSIS IN NEW YORK STATE: REPORT OF TWO NEW CASES AND TABULATED DISCUSSION OF TWENTY-SIX PREVIOUS ONES** GEORGE M. LEIBY, MARION B. SULZBERGER and RUDOLF L. BAER, *Arch Int Med* **75** 145 (March) 1945

Leiby, Sulzberger and Baer tabulated data covering 26 cases of proved or presumptive sporotrichosis previously reported in the state of New York. They describe 2 additional cases, 1 of which was clinically typical and 1 atypical in localization and appearance, involving an upper eyelid. They believe that such atypical and rudimentary sporotrichosis may often escape diagnosis and that infections with sporotrichum fungi may be more common in the state of New York than is indicated by the number of published reports. They state that the intracutaneous test with sporotrichum is a valuable aid in early diagnosis and should be employed in all cases of suspected sporotrichosis, in addition to the usual cultures.

**ESOPHAGEAL CARCINOMA IN BRITISH WEST INDIAN AND PANAMANIAN NEGROES: A STUDY OF THE INCIDENCE, ETIOLOGIC FACTORS AND PATHOLOGIC ANATOMY IN FIFTY CASES** WRAY J. TOMLINSON and LESTER A. WILSON JR., *Arch Path* **39** 79 (Feb) 1945

Carcinoma of the esophagus is common in the Negroes of the British West Indies. Among 50 patients, 26 had clinical and autopsy evidence of syphilis (1 had associated leukoplakia). The average incidence of syphilis was 87 per cent in the autopsy material under consideration.

LYNCH, St Paul

**PROPIONATE AND UNDECYLENATE OINTMENTS IN THE TREATMENT OF TINEA PEDIS AND AN IN VITRO COMPARISON OF THEIR FUNGISTATIC AND ANTIBACTERIAL EFFECTS WITH OTHER OINTMENTS** EDMUND L. KEENEY, LIBERO AJELLO, EDWIN N. BROYLES and ELSIE LANKFORD, *Bull Johns Hopkins Hosp* **75** 417 (Dec) 1944

In an interesting study stimulated by the previous work of Peck and Hopkins, the authors record the clinical effectiveness of propionate-propionic acid ointment and of undecylenate-undecylenic acid ointment in the treatment of tinea pedis. They compared the in vitro fungistatic and antibacterial effects of the propionate-propionic acid ointment and of the 5 and 10 per cent undecylenate-undecylenic acid ointments with those of half and full strength ointments of benzoic and salicylic acid, 10 per cent ammoniated mercury, 5 per cent sulfathiazole and 0.5 per cent tyrothricin.

Tested in vitro on an especially resistant strain of *Trichophyton gypseum*, the propionate-propionic acid was superior to all the other ointments mentioned. The antibacterial effect on *Staphylococcus aureus* and on beta hemolytic streptococci was likewise greatest with the propionate-propionic acid ointment.

This ointment as well as undecylenate-undecylenic acid ointment does not produce irritation or sensitization in clinical use. Further, these ointments have the additional qualifications of fungistatic or fungicidal activity, antibacterial effect and penetration.

The authors feel that use of either of these fatty acid ointments in the treatment of tinea pedis is an improvement over any method of treatment in use at the present time.

NELSON PAUL ANDERSON, Los Angeles

**LUMBAR PUNCTURE HEADACHES** MYRON J LEVIN, Bull U S Army M Dept, November 1944, no 82, p 107

Lumbar spinal punctures were performed on 2,217 syphilitic candidates for induction into the armed forces. The fluids were collected rapidly, the patients immediately got up and were instructed to keep active and not to lie down. Only 15 cases of postpuncture headache severe enough to require rest in bed were reported.

**YAWS IN A WHITE SOLDIER** HAROLD RIFKIN, Bull U S Army M Dept, March 1945, no 86, p 81

The patient was a 29 year old white soldier who had been on duty for one year in various islands in the South Pacific on which natives are known to have yaws. Two months prior to his admission to the hospital he had "stuck a splinter in the middle finger of his right hand," and thereafter an ulcer developed at the site. The soldier had played with native children but denied that he had had sexual contact during the entire stay in this area. On admission to the hospital he had an ulcer 12 mm in diameter on the volar aspect of the distal phalanx of the middle finger of the right hand and a maculopapular eruption on the palms, soles, chest and abdomen. A dark field examination of the ulcer revealed an occasional spirochete, and spirochetes resembling *Treponema pertenue* were found in sections of skin and lymph nodes. The Kahn reaction of the blood was reported as 4 plus positive.

The patient was given oxophenarsine hydrochloride twice a week and a bismuth preparation once a week. After the third injection of the arsenical the Kahn reaction became negative and the ulcer was healing. The ulcer was healed after the fifth injection of oxophenarsine hydrochloride. The patient was given a total of eleven injections of oxophenarsine hydrochloride and three of the bismuth drug. The enlargement of lymph nodes was gone at the completion of this course of therapy, the cutaneous lesions had undergone involution, and the Wassermann reaction was still negative three months later.

**TREATMENT OF YAWS WITH PENICILLIN** RICHARD WHITEHILL and ROBERT AUSTRIAN, Bull U S Army M Dept, March 1945, no 86, p 84

The authors treated 17 patients with primary and secondary yaws from which *Treponema pertenue* was isolated by dark field examination. Most of the patients were given a total of 400,000 to 500,000 units of penicillin over a period of five days. The organisms disappeared from the cutaneous lesions within sixteen hours in 16 cases and within forty hours in 1 case.

Penicillin therapy brought about complete healing within three weeks of all the cutaneous manifestations of yaws with the exception of one lesion which failed to epithelialize because of local scar formation.

During the short period of observation penicillin did not affect significantly the Kahn reaction of the serum.

STRAKOSCH, Denver

**RUBELLA AND CONGENITAL MALFORMATIONS** EDITORIAL, Internat M Digest 46.50 (Jan) 1945

In this editorial, attention is called to several reports in the literature of congenital malformations occurring in infants born of mothers who had rubella during pregnancy. The malformations are serious, occurring usually in the form of cardiac lesions or ocular lesions, particularly congenital glaucoma with resulting blindness. There have been relatively few published reports, but a number of cases have been observed, and they indicate that the incidence of malformations is close to 100 per cent when the rubella occurs in the early months of pregnancy. The question is raised as to the justification of therapeutic abortions in such cases or in any case of virus disease occurring early in pregnancy.

RATTNER, Chicago

**RECENT TRENDS OF LEPROSY IN THE UNITED STATES.** RALPH HOPKINS and G H FAGET, J A M A 126: 937 (Dec 9) 1944

During the last fifteen years 723 patients have been studied in the National Leprosarium. Serologic tests were of little value in the differentiation of leprosy from syphilis but were of some value as an index of the prognosis and of the progress of leprosy. Promin (p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) and diasone (disodium formaldehyde sulfoxylate diaminodiphenylsulfone) proved to be the most beneficial of the numerous experimental drugs investigated. Nephritis and tuberculosis were the direct cause of almost half of the 190 fatalities.

**HODGKIN'S DISEASE** S R BERSACK, J A M A 126: 1025 (Dec 16) 1944

Bersack reports a case of Hodgkin's disease of the skin with terminal spread through the blood stream. The absence of any evidence of dissemination of embolic cellular element is consistent with a virus causation of Hodgkin's disease.

**OCCUPATIONAL DERMATITIS CAUSED BY GERMICIDAL POWDER "MICROLENE"** ALEXANDER STERLING, J A M A 127:219 (Jan 27) 1945

A severe dermatitis of four years' duration involving hands and forearms occurred in a waitress from indirect contact with a germicidal chemical powder, Microlene, used in a dishwashing machine. A patch test with Microlene elicited a strongly positive reaction.

**TREATMENT OF VINCENT'S ANGINA WITH SULFATHIAZOLE.** WILLIAM W MANSON and IRWIN T. CRAIG, J A M A 127:277 (Feb 3) 1945

A total of 48 patients with Vincent's angina were treated with sulfathiazole, without recurrences. The treatment consisted of 1 sulfathiazole tablet (0.5 Gm) dissolved on the tongue every two hours during the day and 2 such tablets dissolved in the same manner every four hours at night. The treatment was continued for a total of seventy-two hours.

**SKIN-HAZARDS IN MANUFACTURE AND PROCESSING OF SYNTHETIC RUBBER** LOUIS SCHWARTZ, J A M A 127:389 (Feb 17) 1945

Comparatively little dermatitis occurs in persons engaged in the manufacture of synthetic rubber. Workers in this industry take a shower bath immediately after



completing the job, then remove protective clothing and don their street clothes

OVERTREATMENT DERMATITIS L E GAUL, J A M A 127 439 (Feb 24) 1945

When the routine dermatologic history of a patient is taken, the previous treatment is recorded in sequence. Patch tests are performed with previously tried medicaments as well as with other suspected contactants. During the interim compresses of sodium chloride solution or a colloidal clay lotion or paste is applied. The post-treatment patch test reduces the incidence of overtreatment dermatitis.

PENICILLIN IN THE TREATMENT OF INFANTILE CONGENITAL SYPHILIS R V PLATOU, ALLEN J HILL, NORMAN R INGRAHAM, MARY S GOODWIN, ERLE E WILKINSON and ARVID E HANSEN, J A M A 127 582 (March 10) 1945

Sixty-nine infants with manifest early congenital syphilis were treated with sodium penicillin. Penicillin was administered intramuscularly in isotonic solution of sodium chloride every three hours in sixty injections over a seven and one-half day period. Total doses used ranged from 16,000 to 32,000 Oxford units per kilogram of body weight. Three infants died during or soon after treatment. All of these had active syphilitic lesions, were under 2 months of age and were in poor general condition. Thirty-nine infants were followed from four to twelve months. Twenty-five of these now are physically normal and have doubtful or negative serologic reactions (21 negative and 4 doubtful). Serologic relapse occurred in 5 infants and clinical relapse in 2 of these 5. The results obtained in this series were not entirely satisfactory. Accordingly, the authors recommend temporarily a total dose of 40,000 Oxford units per kilogram of body weight, given in sixty intramuscular injections over a seven and one-half day period.

STATUS OF POISON IVY EXTRACTS F A STIVINS, J A M A 127 912 (April 7) 1945

It is highly probable that urushiol is the irritant in poison ivy, sumac and the lac trees. Dermatitis venenata is the result of contact after previous exposure and sensitization to the active substance in the plants. Persons who show strongly positive cutaneous reactions with ivy extracts and who are susceptible to the dermatitis can be rendered dermally insensitive to the test and also resistant to rigorous exposure to the plants by the daily ingestion of large increasing doses of ivy extracts. These subjects are desensitized rather than immunized. Most are only temporarily "resistant" to or "protected" against ivy. So far none of the potent extracts for oral therapy have been marketed. There is no satisfactory evidence that the cutaneous reaction or the resistance to poison ivy on rigorous exposure has ever been modified, except by the aforementioned procedure, a procedure which its instigators imply is probably unsafe except under experienced supervision and probably not worth while because the resistance seems but temporary. There is clinical evidence that intramuscular inoculations have conferred resistance on susceptible persons. Since the cutaneous reaction has not been modified and the inoculated subjects have not been rigorously exposed under supervision, some doubt is cast on the validity of the evidence purporting to show protection afforded by intramuscular inoculation. The treatment of the acute rash with ivy extracts should

be discouraged because many patients are made worse and there is no satisfactory evidence that any are helped.

"DIAPER RASH" DUE TO PERM-ASEPTIC WILLIAM L DOBBS, J A M A 128 281 (May 26) 1945

Five cases of diaper rash caused caused by Perm-Aseptic are reported. It is used in the last rinse by diaper services. The purpose is to make textiles actively antiseptic as a protection to persons and as a preventive of destruction of textiles by bacteria, germs, mold and mildew. Patients wore the diapers treated with Perm-Aseptic for at least two months before symptoms of sensitivity appeared.

HENSCHEL, Denver

THE SPIROCHETICIDAL ACTION OF PENICILLIN IN VITRO AND ITS TEMPERATURE COEFFICIENT HARRY EAGLE and ARLYNE D MUSSELMAN, J Exper Med 80 493 (Dec) 1944

Experiments were performed in an attempt to demonstrate the mode of action of penicillin in the treatment of syphilis. Penicillin was found to be actively spirocheticidal in vitro against several strains of nonpathogenic *Treponema pallidum*. Although rendered non-viable, the organisms remained motile for eight to twenty-four hours. The rate of killing by penicillin increased with temperature in the range 8 to 40 C.

THE ROLE OF THE LYMPHOCYTE IN ANTIBODY FORMATION T N HARRIS, E GRIMM, E MERTENS and W E EHRLICH, J Exper Med 81 73 (Jan) 1945

Previous observations by two of the authors had suggested that the lymphocyte may play an important role in antibody formation. The present report deals with confirmatory observations.

LYNCH, St Paul

THE EFFECT OF TUBERCULOUS AND SENSITIZED SERA AND SERUM FRACTIONS ON THE DEVELOPMENT OF TUBERCLES IN THE CHORIO-ALLANTOIC MEMBRANE OF THE CHICK EMILY W EMMART and FLORENCE B SEIBERT, J Immunol 50 143 (March) 1945

The authors made electrophoretic analyses of the amount of albumin and alpha, beta and gamma globulins present in tuberculous, "sensitized," and normal rabbit serums. They then implanted these whole serums simultaneously with tubercle bacilli of the A 27 strain on the chorioallantoic membranes of 8 day old chick embryos. The incidence of membranes in which tubercles developed was calculated and the size and development of the tubercles noted. Under these experimental conditions, serums either from rabbits sensitized with a purified tuberculin protein preparation or from tuberculous rabbits possessed tuberculostatic activities in the chick membrane. Both types of serums had higher gamma globulin contents than serums from normal rabbits. Serums from sensitized rabbits implanted on the chick membrane the day before inoculation with tubercle bacilli also produced partial inhibition of the development of the tubercles in the chick membrane. A gamma globulin fraction isolated from pooled "sensitized" rabbit serums caused partial inhibition of tubercle development while the remaining protein fraction did not. There was a suggestion of partial tuberculostatic effect due to a gamma globulin fraction isolated from pooled serums of patients with minimal tuberculosis, although the data were insufficient to be statistically significant.

**BACTERIAL DESTRUCTION OF NICOTINIC ACID** STUART  
KOSER and GRACE ROSSKOFF BAIRD, J Infect Dis  
75 250 (Nov-Dec) 1944

Little is known about the capacity of bacteria to accomplish the destruction of vitamins. Most microbiologic work dealing with accessory factors has been concerned with the nutritive requirements of various bacteria, yeasts or higher fungi, with the use of microorganisms for vitamin assay procedures or, more rarely, with their use as "tools" to study the function of vitamins. In the present investigation, the authors studied the decomposition of nicotinic acid, paying particular attention to the bacteria capable of growing in a medium containing this vitamin as the only organic compound.

They found that bacteria of the green fluorescent pigment-producing group, *Pseudomonas fluorescens* and allied types, and also *Serratia marcescens* and related species are able to grow in a simple synthetic medium containing nicotinic acid as the only organic compound. Low concentrations of nicotinic acid support growth while amounts of from 0.5 to 1 per cent often delay growth or inhibit it entirely. Destruction of nicotinic acid, as measured by the chemical method, occurs during cell multiplication. When 0.1 per cent nicotinic acid is supplied, often 95 per cent or more of the vitamin is utilized; in the presence of 0.5 per cent nicotinic acid, a smaller proportion of the total amount is destroyed.

Many cultures fail to grow or grow but poorly when nicotinamide is substituted for the acid. All cultures fail to grow when the isomers isonicotinic and picolinic acids are supplied in place of nicotinic acid. Several other derivatives are utilized less readily than nicotinic acid. Both groups of bacteria causing the breakdown of nicotinic acid also synthesize the vitamin when grown in mediums originally devoid of it. The results emphasize the broader field of destruction of vitamins by bacteria, in contrast to the better recognized role of vitamins as coenzymes or accessory factors.

NOTE BY ABTRACTOR—Nicotinic acid is found in sweat. The subject matter discussed here should furnish a lead for investigating the action of fungi imperfecti on sweat and the possibilities for the use of this information in therapeutic measures.

**THE INFECTION OF TICKS (DERMACENTOR VARIABILIS) WITH PASTEURILLA TULARENSIS** J. FREDERICK BELL,  
J Infect Dis 76:83 (March-April) 1945

Present methods for the control of tularemia are not founded on an understanding of the ecology of the disease. In this study an attempt, based principally on analogy with the results of similar studies on plague, was made to determine the nature of the barriers to the spread of tularemia among ticks. Individual variations in susceptibility to infection was a possible cause of lack of uniformity of infection in ticks of an exposed group, and it is suggested that increased susceptibility to infection might result from decreased vitality, but the subject was not carefully investigated. Bacteriophage was not discovered in any of the experiments.

In the few samples tested the fecundity of infected ticks, as measured by the production and fertility of ova, was not diminished, nor was viability adversely affected.

The data indicate that the epizootic course of tularemia does not depend merely on a large number of ticks and the presence of many suitable hosts, and "hereditary" transmission does not appear to be of significance for *D. variabilis* as no evidence of infection thus

transmitted was obtained. "Hereditary" transmissions, therefore, may be the exception rather than the rule in nature, and the lack of it would be a most important limiting factor.

That 1 rabbit that was fed on by several hundred infected ticks did not die or even become ill of tularemia was ascribed to the fact that the animal had previously been fed on by ticks and probably had developed an immunity to the parasite which acted in a nonspecific way (probably through a cellular mechanism) to prevent infection.

The author demonstrated that infected ticks feeding on immune or normal hosts lose their infection, presumably as a result of the stimulating effect of the blood meal in a normal bactericidal function of the tick's gut, but, before losing their infection as a result of feeding, infected ticks may inoculate the host, whereupon the host, if it is not immune, will acquire septicemia and infect all ticks feeding on it. Infected ticks feeding on immune hosts, on the other hand, permanently lost their infections and the bacteria were not transmitted to normal ticks feeding concurrently.

Since the blood meal causes eradication of infection already present in ticks, Bell advances the theory that organisms acquired by feeding on the blood of animals with septicemia are not also destroyed because a factor is present in normal blood which is complementary to and necessary for the action of the bactericidal element resident in the tick; he further supposes that septicemia removes this hypothetical factor from the blood, thus permitting invasion of the ticks by the organisms. The importance of immune animals in limiting the spread of tularemia is indicated by these experiments. The feeding of ticks was greatly facilitated by heightened temperature of the environment. The enhancement of the normal bactericidal principle present in ticks at high temperatures, according to the law of Van Hoff, could not be demonstrated in regard to the survival of infecting bacteria in nymphs of *D. variabilis*.

CORNBLEET, Chicago

**ALLERGY FROM TIMBO (LONCHOCARPUS H.B.K.)** A  
OLIVERIA LIMA, J Lab & Clin Med 29 939 (Sept)  
1944

This is a report of the case of a Brazilian man in whom after exposure to an insecticide and to flora of the Amazon region, asthma and a dermatitis of the contact type developed. He became allergic at the same time to the atopic and resinous principles of timbó. The author was able to demonstrate by a series of scratch, intradermal and patch tests that the patient was sensitive to both timbó and Derris (cubé). The atopic and contact principles of the two genera belong to two different classes of substances. The timbo belongs to the genus *Lonchocarpus* and derris to the Leguminosae family. The eczematous eruptions occurred only when the crude extracts of the *Lonchocarpus* and derris leaves were used. The eruption did not appear when the resinous principle of leaves and roots of the plants were extracted with ether. On studying the antigenic behavior of the atopic principle of the two genera by means of Dale test (sensitized uterine strips), the author was able to demonstrate an immunologic relationship between the water-soluble antigens of timbó and derris.

AN ALKALINE MEDIUM AND PROCEDURE FOR THE SELECTION OF DERMATOPHYTES IN THE PRESENCE OF SAPROPHYTIC FUNGI J M LEISE and L H JONES, *J Lab & Clin Med* **30** 119 (Feb) 1945

The purpose of this study is the selection of a medium of proper  $pH$  in which pathogenic fungi (dermatophytes) could grow and be identified by suppressing the growth of the more rapidly growing saprophytic fungi

In this study the authors found that in the growing of a mixed suspension of dermatophytes and saprophytic fungi the best results were obtained when they used poured plates of alkaline medium of Sabouraud's maltose agar of  $pH$  10.5 incubated five and one-half days at 34 C. Under these conditions, the inhibition of the saprophytic growth was greater than the inhibition of dermatophytes. A fluctuating room temperature was found to be more inhibitory for the dermatophytes.

There was an overgrowth of saprophytes in cultures over five and one-half days old. Plates which were negative for pathogenic fungi after the five and one-half days were further incubated for about ten days, with daily observation. Colonies that were thought to be pathogenic were transferred to suitable mediums for purification and examination.

The authors think that the effectiveness of the alkaline medium in selecting dermatophytes when in the presence of saprophytic fungi may be due to the presence of a trypsin-like enzyme system in the dermatophytes. The presence of such an enzyme system and the resultant ability to grow in highly alkaline substrates may be a characteristic of pathogenic fungi and bacteria and of pathogenicity itself.

The alkaline medium and culturing procedure may be used in the isolation of dermatophytes from infected skin, worn shoes and floors.

The historical review incorporated in this study is extensive and comprehensive. GEIBLER, Los Angeles

DERMATOLOGIC DISEASES FREQUENTLY ENCOUNTERED BY OTOLARYNGOLOGISTS A B CANNON, *New York State J Med* **44** 1661, 1944

Cannon discusses various forms of stomatitis and cheilitis resulting from dentifrices, lipstick, self biting and licking, phenolphthalein or other laxatives, vitamin deficiencies, leukoplakia, lichen planus, carcinoma, gumma and pemphigus. A brief outline of diagnosis and treatment is given.

EPITHELIAL CYSTS F A DOLCE and R L CLARK, *New York State J Med* **44** 2358, 1944

The authors describe 4 cases of epithelial cysts of the palms. The differential diagnosis between ganglions, fibromas and sebaceous cysts is discussed. Complete surgical removal is the treatment of choice.

THE WAR AND OXYGEN THERAPY J H EVANS, *New York State J Med* **44** 2443, 1944

After discussing oxygen therapy by inhalation, Evans describes subcutaneous oxygen therapy as being beneficial for local infections, arthritis in its acute stage, ringworm and burns, for relief of pain following dislocations and sprains and for promoting the healing of wounds. Mechanically it may act as follows: (1) opening up compressed lymph channels and providing better drainage, (2) serving as a buffer for inflamed tissues, thus relieving pain, and (3) improving local

circulation of the blood. Evans reports that a few patients with ringworm were treated by subcutaneous oxygen therapy and that this method helped in the clearing up of bloody discharge and the healing of ulcerations.

INTENSIVE TREATMENT OF EARLY SYPHILIS-METHOD OF EAGLE AND HOGAN G M MACKEE and G D ASTRACHAN, *New York State J Med* **44** 2577, 1944

The Eagle and Hogan method consists of tri-weekly injections of oxophenarsine hydrochloride for a total of six, eight or ten weeks, the dose being approximately 1 mg per kilogram of body weight. Bismuth compounds may be given concurrently once a week. This treatment was given to 61 patients. Primary and secondary lesions healed in an average of twelve and six-tenths and seventeen and six-tenths days, respectively. In 58.8 per cent of the cases the serologic reactions were reversed completely to negative. The untoward reactions were in most of the cases of a mild character. The treatment had to be discontinued because of the severity of reactions in only 7 cases. This method is still in the experimental stage, and it should be used cautiously when one is dealing with cooperative patients.

CHICKENPOX, HERPES ZOSTER AND ACUTE ANTERIOR POLIOMYELITIS J C MCGARRAHAN, *New York State J Med* **45** 193, 1945

The author discusses the interrelationship between chickenpox and herpes zoster and presents a method of treatment (intravenous injection of thiamine hydrochloride) which was used in a case of chickenpox. It brought the disease to an abrupt end in six hours.

RONCHESE, Providence, R I

CHANCROID OF THE CERVIX LOIS A DAY, *Proc Staff Meet, Mayo Clin* **20** 70 (March 7) 1945

Two cases of chancroid of the cervix are reported. In 1 of these cases the patient's husband acquired a chancroid in January 1944, while in the tropics, and was treated with a sulfonamide compound. His lesion rapidly underwent involution. He returned home in September, and five days later symptoms of chancroid developed in his wife. Examination of the husband did not reveal a lesion of the genitalia, and smears and cultures from the glans penis and prostatic cultures failed to demonstrate the presence of *Hemophilus ducreyi*. P A O'Leary, in discussing this case, states that the husband is a carrier of the organism, although its presence cannot be demonstrated. It has been known for some time that women may be carriers of *H. ducreyi* without demonstrable lesions, but it is rare that a man has been suspected of transmitting the disease in the absence of ulcerative lesions of the genitalia. Both patients responded to sulfathiazole administered by mouth and locally. In 1 of the patients intolerance to the sulfonamide drug developed, and penicillin was used advantageously. Zephiran chloride is the most efficient prophylactic agent against *H. ducreyi*.

HENSCHEL, Denver

A CONTRIBUTION TO THE TREATMENT OF POST-IRRADIATION NECROSIS JOHN E MOSELEY, *Radiology* **44** 262 (March) 1945

The author reports 2 cases of radiation necrosis successfully treated with estrogenic ointment. Others to report good results in the treatment of radiation

necrosis with estrogenic hormones in oil are Sellers and Wagner. The rationale for such therapy is based on the fact that follicular hormones have a vasodilating effect on the smallest blood vessels of the skin and also have a selective growth-promoting action.

CIPOLLARO, New York

VALUE OF SULFONATED OILS IN THE TREATMENT OF BURNS AND OTHER DENUDED SURFACES. WILLIAM L. ROGERS, THEODORE M. COHEN and RAYMOND R. GOLDBERG, U S Nav M Bull 42 1125 (May) 1944

In cases of burns in which the initial shock is slight and facilities for primary debridement are available, the use of sulfonated oils was extremely effective for rapid cleansing of involved areas with negligible trauma.

When a patient is in severe shock, the authors use a spray film preparation of the following formula:

|                              | Gm or Cc |
|------------------------------|----------|
| Paraffin wax                 | 265      |
| White wax                    | 215      |
| Sulfonated liquid petrolatum | 330      |
| Sodium lauryl sulfate        | 10       |
| Water                        | 30       |
| A sulfonamide compound       | 50       |
| Triethanolamine              | 100      |

The advantages claimed for this preparation are:

(1) ease of application, (2) rapid removal of grease and dirt on subsequent washing, (3) chemotherapeutic agent available for absorption, (4) stimulation of granulating surfaces and (5) ability to treat large numbers of casualties quickly.

STUDIES ON FILARIASIS IN THE SAMOAN AREA. ELTON E. BYRD, LYLE S. STAMANT and LEON BROMBERG, U S Nav M Bull 44 1 (Jan) 1945

Through laboratory and field studies convincing evidence was found that the mosquito *Aedes scutellaris* var. *pseudocutellaris* is the important transmitter of filariasis within the Samoan area. Since this species has a very short flight range, the authors suggest that military camps should never be quartered less than 500 yards (450 meters) from the nearest native habitation. Other precautions to be observed are: (1) complete isolation from native habitation, (2) prevention of natives from entering camp, (3) orders prohibiting troops from entering native villages during daylight, because of "day biting" habits of the mosquito hosts, and (4) the use of screened quarters and bed nets as standard items of equipment.

OUR LEPROSY PROBLEM. GEORGE M. SAUNDERS, U S Nav M Bull 44 54 (Jan) 1945

In a timely article, the author states that leprosy will soon become an American problem because an appreciable number of infections will develop among the troops who have served in endemic areas. He covers the subject thoroughly, discussing world distribution, etiology, clinical findings, diagnosis, treatment and prevention and control.

It is reemphasized that although there is no specific treatment for leprosy, almost all patients show improvement with adequate diet, rest and suitable exercise. Other methods useful in controlling symptoms and complications are: (1) sulfonamide compounds for the treatment of secondary infections which complicate ulcerative lesions, (2) thiamine hydrochloride for relief of a painful neuritis, (3) surgical intervention to remove necrotic bones, and (4) tracheotomy for patients with tracheal involvement.

SALT WATER ULCERS OF THE EXTREMITIES—OCCURRENCE IN JAPANESE SURVIVORS. CHARLES W. McLAUGHLIN JR. and JAMES L. HOLLAND, U S Nav M Bull 44 494 (March) 1945

An unusual type of ulcers on the extremities was observed in 13 Japanese survivors rescued in the South Pacific. These lesions in the early stages appeared as small vesicles or blisters, followed by gangrene and sloughing, leaving ulcers which varied from 0.5 to 3 cm in diameter. The final lesions appeared as deep circular or oval punched-out ulcers with precipitous edges and a pinkish-gray granulating base. The surrounding areas were free from any inflammatory reaction, but the edges were extremely sensitive. A temperature of 99 to 101 F. was invariably present when involvement was extensive. Repeated smears revealed gram-positive cocci in pairs and clumps. Healing was slow, and no difference in time was noted from the use of sulfonamide and other antiseptics and of dry sterile dressings.

The authors felt that these lesions were similar to the so-called "tropical ulcers" or "desert sores" and that trauma with exposure to salt water was the etiologic factor in the production of these ulcers.

GRANULOMA INGUINALE. JOHN G. MENVILLE, U S Nav M Bull 44 621 (March) 1945

The author observed 4 cases of granuloma inguinale occurring in areas other than the inguinal region.

One atypical case is reported in which the disease began in a young Negro man as a penile lesion one week after sexual exposure. At the end of three weeks, the "pimple" enlarged into a rounded, button-shaped, flat, nontender red lesion, 2.5 cm in diameter, located adjacent to the coronal sulcus and to the right of the frenulum.

Repeated dark field examinations and Kahn tests of the blood did not reveal syphilis. Microscopic examination of scrapings and a biopsy specimen were negative for leishmania bodies.

Treatment consisted of injection of 3 cc of 1 per cent antimony and potassium tartrate intravenously the first day, the amount being increased 1 cc each day until a total dose of 10 cc was reached. The lesion showed improvement after the fourth injection and was completely healed in eighteen days.

RODIN, South Bend, Ind

SKIN-ERUPTIONS DUE TO THE LOCAL APPLICATION OF SULPHONAMIDES. G. A. GRANT PETERKIN, Brit J Dermat 57 1 (Jan-Feb) 1945

The author reports 65 cases of light eruption due to the external application of sulfonamide drugs. Thirty-two of the patients had been treated for impetigo, 8 for impetiginized seborrheic dermatitis, 3 for septic infection of the limbs, 2 for secondarily infected tinea of the feet, 5 for "running ears" (otitis externa), and 15 for wounds and burns of the limbs. In all but 4 cases the first sulfonamide drug to be applied was sulfanilamide powder. It is suggested that the eruption is invariably, or almost invariably, preceded by application of the powder and that the patient becomes sensitized to the drug by its inhalation. It is urged that powdered sulfonamide compounds should not be applied to the skin for minor conditions.

Over 200 patients, including 183 with impetigo or impetiginized seborrheic dermatitis, were treated in North Africa with 5 per cent sulfathiazole in paste of

zinc oxide or Lanette wax cream and the skin freely exposed to light. Only 1 patient (with respirator dermatitis) had the eruption described, but this was mild and soon subsided. It is considered that 5 per cent sulfathiazole in a suitable base is probably as safe as such drugs as ammoniated mercury for dermatologic therapy and gives better results. A comparison is made between this eruption and other light dermatoses, such as Hutchinson's summer prurigo and pellagra.

THE INCIDENCE AND LOCALIZATION OF ACNE. E. LIPMAN COHLN, *Brit J Dermat* 57 10 (Jan-Feb) 1945

The author reports on the incidence of acne in a group of 500 women. The maximum incidence occurs at the ages of 19 to 21 years, but the disease is still common in the late twenties and early thirties. The age incidence in a group of men with acne was also studied and the largest group was 18 to 23 years old, but 25 per cent of the patients were over the age of 25 years. The author is of the opinion that most writers put the upper age limit of acne too low. In a study of the distribution of acne in a group of women the chin region was found to be far the most common site.

BIUFARB, Chicago

PREVENTION OF POST-ARSPHINAMINE JAUNDICE. J. BEATTIE and J. MARSHALL, *Brit M J* 2 651 (Nov 18) 1944

An attempt has been made to control the occurrence of damage to the liver in syphilitic patients under treatment with neoarsphenamine.

Sulfur-containing amino acids were given during that period of treatment when the expected incidence of hepatic damage was maximal.

Four preparations were tested—casein digest, casein digest reinforced with cystine, cystine and methionine.

These preparations had no effect on the over-all incidence of hepatic damage. Certain of them, however, were noticeably effective in (a) shifting the time of peak incidence of hepatic damage toward the end of the second course of antisyphilitic treatment or later and (b) moderating the severity of the damage when this did occur. The effect of the casein digest reinforced with cystine was less than that of an equivalent quantity of synthetic methionine. Cystine produced an effect similar to that of methionine only when given in large quantity on the day of the injection of the arsenical.

It was concluded that men undergoing antisyphilitic treatment should receive dietary supplements as a prophylactic measure against attacks of jaundice.

These supplements should not take the form of large quantities of cystine as this procedure may reduce the chances that the antisyphilitic treatment will be successful.

PENICILLIN PASTILLES FOR ORAL INFECTION. A. B. MACGREGOR and D. A. LONG, *Brit M J* 2 686 (Nov 25) 1944

Penicillin included in a pastille under suitable conditions is liberated in the mouth in an active form, and

the concentration in the mouth can be maintained without ill effects.

Acute ulcerative gingivostomatitis (Vincent's type) is simply, quickly and effectively treated in this manner. When this disease was treated in the acute stages, no recurrences were seen over a three and one-half month follow-up period.

Acute hemolytic streptococcal tonsillitis seemed to respond clinically to treatment with pastilles containing penicillin.

SULPHONAMIDE ALLERGY. THE PERSISTENCE OF DESSENSITIZATION. R. G. PARK, *Brit M J* 2 816 (Dec 23) 1944

The author describes two types of allergic sensitivity which can arise during sulfonamide therapy—according to whether the drug is taken internally or is applied to the skin. The internal type may take many different clinical forms, of which fever, morbilliform erythema and leukocytosis are the commonest features. In the cutaneous type the reaction is an eczematous dermatitis. In either case violent reactions are apt to follow administration of the drug by mouth.

The author feels that he has successfully desensitized his patients by giving gradually increasing amounts of the drug by mouth. For patients with the internal type it is usually possible to start with 0.1 Gm at each dose, doubling up daily to reach 1 Gm in four or five days. For more sensitive patients desensitization may take longer.

In persons with the eczemas a high degree of sensitivity is the rule, requiring a starting dose of 0.005 Gm and about six weeks to desensitize. In 1 case re-investigation after one year showed that the allergy had partially returned but to only a fraction of its original level.

PENICILLIN IN CIVILIAN PRACTICE. H. B. MAY, *Brit M J* 2 817 (Dec 23) 1944

The author feels that local treatment of staphylococcal diseases of the skin with penicillin will be of great value in suitable cases.

In the treatment of sycosis a lotion was less effective than a cream which is prepared with a concentration of 200 units per gram of a base made of sterile Lanette wax and castor oil which had been autoclaved. The sterile base is prepared in large quantities, and the penicillin is added as needed.

A self-sterilizing cream is not available as yet. Tablets of penicillin proved easier to handle and more economical to use than ampules.

TWO CASES OF ERYSIPELOID TREATED BY PENICILLIN. G. A. HODGSON, *Brit M J* 1 483 (April 7) 1945

Two army cooks were infected with erysipeloid after butchering a calf. Both had open wounds on their fingers, and by the eighth day of illness the clinical pictures of the two men were identical.

Each received sodium penicillin intramuscularly until totals of 485,000 units and 560,000 units had been given. Improvement was prompt, and by the fifth day both men were practically well.

SHAW, Chattanooga, Tenn.

## Society Transactions

### CENTRAL STATES DERMATOLOGICAL SOCIETY

Meeting Held Under the Auspices of the  
Cleveland Dermatological Society

JAMES R DRIVER, M D, *President*

GEORGE W BINKLEY, M D, *Secretary and Reporter*

*April 29, 1944*

#### Bowen's Disease of Penis, Late Latent Syphilis (Treated) Presented by DR JAMES STRAUCH and DR S COLIMODIO

R M, a Negro aged 51, was previously presented before the Cleveland Dermatological Society from the department of dermatology, University Hospitals, as "A Case for Diagnosis (Chronic Balanoposthitis?)"

The penile lesions have shown no real change in the past four years. The glans penis continues to exude and is painful.

A second biopsy was made on Jan 9, 1941. Sections showed hyperkeratosis and patchy parakeratosis. There was definite acanthosis. Rete pegs were elongated. There was variation in the appearance of cells of the malpighian layer. There were many vacuolated cells with eccentrically placed nuclei and others decidedly swollen. Some cells had circular, deeply chromatic, irregularly shaped nuclei that were surrounded by small clear spaces. The nuclei were hyperchromatic. There were many atypical mitotic figures.

Numerous lymphocytes and large round cells infiltrated the dermis. The major portion of the specimen consisted of dense connective tissue in which there were focal collections of lymphocytes and plasma cells.

Antisyphilitic therapy was begun in 1940 but was interrupted after twenty injections of a bismuth preparation and ten of oxophenarsine hydrochloride. A bismuth dermatitis appeared.

#### DISCUSSION

DR ISAAC J ARNISON, Buffalo. To me this looks clinically as well as histologically like balanitis xerotica, although there is some vacuolation. Histologically there is absence of the dyskeratosis which would be characteristic of Bowen's disease. To my mind it is a simple balanitis xerotica.

DR B F BARNEY, Columbus, Ohio. I think that this case falls into the category of cases of the disease reviewed and described clinically and pathologically by Dr Stiles following a syphilitic infection. The appearance of the skin and the pathologic picture agree with that diagnosis. I think that it is rather an academic question of whether this is Bowen's disease or erythroplasia. They are essentially the same, but I think that it does fit into the latter classification a little better than into that of Bowen's disease.

DR JAMES STRAUCH, Cleveland. The basis for the clinical diagnosis is Dr Karsner's pathologic diagnosis. I am not sure whether one can differentiate histologically or not. He observed that besides the vacuolation of cells there were numerous deeply chromatic nuclei. Dyskeratosis was present. The inflammatory cells were

most numerous in the connective tissue. The diagnosis was that of Bowen's disease.

DR MYER W RUBENSTEIN, Pittsburgh. I agree with the diagnosis of Dr Barney. I believe that syphilis has no connection with this case.

#### Sarcoidosis, Tuberculoid Leprosy? Late Latent Syphilis (Treated) Presented by DR JAMES STRAUCH and DR S COLIMODIO

F W, a Negro woman aged 43, is presented from the department of dermatology and syphilology of University Hospitals. She was previously presented before the Cleveland Dermatological Society with a diagnosis of sarcoidosis or leprosy (ARCH DERMAT & SYPH 45:824 [April] 1942). There is no family history of any similar disease.

There are raised infiltrated circumscribed slightly nodular plaques, lighter than the surrounding skin, roughly symmetrically distributed on the face, trunk, arms and thighs. The finger joints show a fusiform puffy swelling. There is a verrucous growth on the left ala nasi. The cervical and inguinal lymph nodes are enlarged. The general physical examination revealed normal conditions. There are no areas of hypesthesia.

Tissue removed from the nose, back and arm showed a chronic granulomatous inflammation consistent with Boeck's sarcoid. Special stains revealed no acid-fast bacilli.

She has received a total dose of fifty-three injections of bismuth over a period of twenty-two months with no change in the cutaneous lesions from April 3, 1941 to June 22, 1943.

#### Sarcoidosis Presented by DR JAMES STRAUCH and DR S COLIMODIO

C W, a Negro woman aged 27, is presented from the department of dermatology of the University Hospitals. The patient was first seen, with phlyctenular conjunctivitis, in October 1940. On July 7, 1942, she complained of swelling of the parotid glands for eleven weeks. There were pain in the legs and the appearance of erythematous patches on the anterior surfaces of both lower legs after the use of sulfathiazole. At that time the only significant observation was hard, non-tender enlarged parotid glands. Roentgenograms of the chest and bones revealed normal conditions. One month later, iridocyclitis of the right eye appeared, it cleared up and then recurred one month later.

One sister had typical erythema induratum at the time of the onset of the patient's uveoparotid syndrome. Two years later, she contracted pulmonary tuberculosis, with acid-fast bacilli in the sputum. C W was in close contact with this sister. One brother was rejected by Selective Service because of active tuberculosis.

There is slight bilateral scleral injection present, with keratic precipitates on both corneas. The parotid glands are slightly enlarged. There are erythematous nodular lesions on both legs.

The urine and the hemogram were normal. Complement fixation and flocculation reactions of the blood were negative. The plasma proteins were 6.2 Gm per hundred cubic centimeters. The albumin-globulin ratio was 1:2. Old tuberculin elicited a positive reaction in



a 1:10 dilution, but reactions to higher dilutions were negative

A roentgenogram of the chest made on Oct 14, 1942 revealed enlargement of the right paratracheal lymph nodes. Repeat roentgenograms of the chest over two and one-half years showed regression of the mediastinal enlargement. An interpretation on Jan 12, 1944 was "There still remains bilateral diffuse mottling of the pulmonary fields, probably due to sarcoidosis."

Histologic sections of skin showed granulomatous infiltration throughout the corium with tubercle formation but without caseation.

**Sarcoidosis** Presented by DR CLAUDE L. CUMMER and DR C. G. LAROCO

H. W., a Negro aged 47, from St. Vincent Charity Hospital, was presented before the Cleveland Dermatological Society with a diagnosis of sarcoidosis (*ARCH DERMAT & SYPH* 49:446 [June] 1944).

**A Case for Diagnosis (Sarcoid, Late Cutaneous Syphilid?)** Presented by DR E. W. NETHERTON and DR W. R. HUBLER

W. D., a married man aged 33, came to the Cleveland Clinic Foundation Hospital on March 13, 1944 with a lesion involving the right upper eyelid. His past history was unimportant. However, he states that his father and mother have syphilis and that a sister seven years younger than he has been treated for interstitial keratitis. Before he came to the clinic, five serologic tests for syphilis were made, all of which elicited negative reactions.

Nine months ago, he sustained a painful injury to the right eye, caused by a thrown apple. The trauma did not cause an ecchymosis. The cutaneous lesion for which he is presented developed six weeks later. The right upper eyelid became swollen and red. The lesion developed rapidly but it has not changed in size during the past five or six months. There has been no discomfort, however, the enlarged upper eyelid has partially obstructed the vision of the right eye.

There is a dull red, smooth, disklike plaque of doughy consistency, involving most of the right upper eyelid. On palpation, the plaque consists of a well demarcated infiltration, which extends into the fold of the eyelid. The thickest portion of the lesion involves the margin of the lid. The eyelashes are absent. The lesion has the appearance of a chronic granuloma. There is no telangiectasia and no pearly deposit which is seen in a basal cell epithelioma.

Histologic examination showed the following conditions. The epidermis was normal, except for thinning and obliteration of interpapillary pegs by the infiltrate in the corium. The tissue of the papillary and subpapillary portions was dense and showed a slight amount of lymphocytic infiltration. In the deeper portion of the corium there were poorly demarcated areas of cellular infiltration. The infiltrate was composed of lymphocytes, large mononuclear cells and many plasma cells. Some of the arterial vessels were thickened and partly hyalinized, others showed proliferation of the intima. In a separate section of the subcutaneous tissue, the infiltration located between striated muscle fibers consisted mostly of lymphoid cells. In other areas there were well demarcated nodules composed of large mononuclear and epithelioid cells, partly or completely surrounded by lymphocytes and an occasional plasma cell.

Physical examination shows enlargement of the epitrochlear lymph nodes. There are no other significant changes. The roentgenogram of the chest showed

normal conditions. An intradermal test with 1:100 dilution of old tuberculin elicited a negative reaction. The urine and the hemogram were normal. The Wassermann and Kahn reactions of the blood were negative.

Since March 13, 1944, four roentgen ray treatments of 100 r each with a 1 mm aluminum filter have been given to the lesion on the eyelid. The lesion has decreased in size.

#### DISCUSSION OF FOUR PRECEDING CASES

DR HUGO HECHT, Cleveland. In the case of C. W., the roentgenograms show enlarged paratracheal lymph nodes and the biopsy shows cells with tuberculous inflammation. I regard this as a tuberculid. In the case of H. W. the lesion looks like lupus rather than a sarcoid. The lesion is soft and not indurated, and, through the exclusion of other diagnoses, I should call it lupus tumidus. In the case of W. D., I favor the diagnosis of syphilis rather than that of sarcoid.

DR C. G. LAROCO, Cleveland. With reference to the case of H. W., I refer to the sarcoids seen at St. Vincent Charity Hospital. If the disease were lupus, there should be a sign of ulceration over this long period. The lesion has persisted as a noninflammatory tumor. Roentgenograms of the long bones show conditions consistent with the diagnosis of sarcoid.

DR HOWARD J. PARKHURST, Toledo, Ohio. In the case of C. W., the question arises as to whether the eruption is sarcoid or papulonecrotic tuberculid. In the cases of papulonecrotic tuberculid that I have observed the lesions have had a much more rapid course than these, and there has been scarring after the involvement has been present this length of time. I feel that lesions with the slow course shown by this one are more likely to be lesions of sarcoid. In the case of W. D., I am strongly in favor of sarcoid.

DR STANLEY CRAWFORD, Pittsburgh. In the case of C. W., several things might be thought of, among them lichen obtusus corneus. I did not see much evidence of sarcoid. The patient has an anergy, which is against papulonecrotic tuberculid but is encountered in patients with sarcoid or lichen obtusus corneus. The other cases I think are definitely instances of sarcoid.

DR FRANZ L. BLUMENTHAL, Detroit. I should think that clinically one could not distinguish in the case of H. W. whether the eruption is sarcoid or lupus. I have seen cases of lupus in which there was no tendency toward ulceration. I suggest animal inoculation.

DR JOHN E. DALTON, Indianapolis. The department of internal medicine of the University of Indiana School of Medicine has been following several cases of erythema nodosum with sarcoid infiltration in the lungs. It would be interesting to follow these cases.

DR MYER W. RUBENSTEIN, Pittsburgh. Do the erythema nodosum nodules disappear when the pulmonary lesions clear?

DR JOHN E. DALTON, Indianapolis. They have improved, but they have not completely disappeared. In one of the cases I had, there was a lesion above the clavicle. At the time operation was performed, the lesion was removed. It showed a typical sarcoid structure.

DR HAROLD N. COLE, Cleveland. I am disappointed that there has been no remark regarding the case of F. W. This patient has been under observation for about three years. The process has regressed somewhat. From the illustrations of this patient in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* (45:824-827 [April] 1942) one may see that the lesions were



more noticeable than they are at present. The patient was seen by two leprologists, and both made the diagnosis of tuberculoid leprosy. I was eager to see whether any one would make a diagnosis of leprosy. She has all the characteristics of sarcoidosis. Rabello (Rabello, F. E. *A lepra incompleta no experiencia do Sanatorio Padre Bento, Rev. brasil de leprol* 11: 115-132 [June] 1943) from Brazil, has reported on a series of patients with tuberculoid leprosy showing all the findings of sarcoidosis, including the anergy to tuberculin and the osseous changes. Sometimes it is almost impossible to distinguish between these two diseases.

DR LOREN W. SHAFFER, Detroit. How are they differentiated?

DR HAROLD N. COLE, Cleveland. Of course in the tuberculoid type of leprosy it is almost impossible to find the organisms. The disease is well under control of the patient's immune powers. The patients are supposed not to be dangerous to any one else, and the disease does not cause any trouble. In this particular case the process is gradually regressing.

DR STANLEY CRAWFORD, Pittsburgh. It is the impression in Scandinavia that sarcoid is a form of leprosy, but the world has not accepted that, especially in the southern part of the United States, where the disease is more prevalent.

DR ISAAC J. ARNSSON, Buffalo. If one could go by therapeutic tests, one could consider the difference in response of sarcoid and leprosy. Some of the patients do improve considerably after using chaulmoogra oil. In patients with Boeck's sarcoid regression took place after fourteen injections of chaulmoogra oil. This case certainly looks like one of leprosy. I tried to palpate the nerve around the neck. There was no disturbance of esthesia. I think that the eruption is a sarcoid.

DR C. K. HAYSLEY, Detroit. I think that the radiologists can offer help in the process of sarcoid. There is one living in Detroit now who is particularly interested in this type of sarcoid. If you care to send him any films you may have, he will be pleased to offer any help he can. I also studied the films of the hands, showing areas of erosion from pressure. In Detroit many cases have been found lately, and the radiologists have proved to be right.

DR HARRY L. CLAASSEN, Cincinnati. In regard to the case of F. W., Dr. Cole stated that the patient is improved. In cases in which a sarcoid is improving, usually the sarcoid improves but the patient's physical condition usually becomes worse. Is that true in this case?

DR GEORGE W. BINKLEY, Cleveland. I think that the patient's physical condition has not changed in the past year.

DR JAMES STRAUCH, Cleveland. In regard to the case of F. W. I should like to call attention to the fact that the patient had a positive Wassermann reaction. On that basis antisyphilitic therapy was started. Nothing has appeared in the history of her family. The positive Wassermann reaction may be due to leprosy. In the case of C. W. the family history shows that the patient has a sister who had erythema induratum as well as pulmonary tuberculosis. She also has a brother who has active tuberculosis. She was in close contact with open tuberculosis.

DR E. W. NORTON, Cleveland. Clinically the lesion in the case of W. D., presented by the Cleveland Clinic Foundation Hospital, looks like a granuloma. It

could easily be a gummatous process or a sarcoid. As Dr. Parkhurst has pointed out, the anergy to tuberculin and the repeatedly negative serologic reactions of the blood are against the diagnosis of late cutaneous syphilis. This does not rule out syphilis as a diagnosis, however. Histologically, the lesions consist of areas of cellular infiltration, consisting chiefly of lymphocytes and large mononuclear cells. There are, however, numerous plasma cells. The histologic structure favors the diagnosis of syphilis more than of sarcoidosis.

#### Postsyphilitic Dyschromia, Late Dyschromic Pinta? (Treated) Presented by DR JAMES STRAUCH and DR G. W. BINKLEY

M. K., a white woman aged 64, is presented from the department of dermatology of the University Hospitals. She was presented previously before the Cleveland Dermatological Society as "A Case of Erythroderma of the Hands and Wrists in a Syphilitic Patient" (*ARCH. DERMAT. & SYPH.* 39: 1073 [June] 1939). No history of alopecia, genital sore or inguinal adenopathy was obtained. She has always lived in Cleveland. She has been married to her second husband for twenty-three years. There is one daughter, aged 21, who is living and well and with no syphilis, and three children by the first husband. They are living and well.

One year after antisyphilitic treatment was begun, there remained a glove-like area of uniform pigmentation with slight erythema. At present, six years after the start of therapy, the erythroderma has disappeared, leaving slight hyperpigmentation on the dorsum of the hands and various areas of depigmentation on the flexor surfaces of the forearms. There are sharply defined triangular areas of depigmentation on the flexor surfaces of the wrists. The base of each triangle is at the level of the wrist joint. Cigarette-paper-like superficial atrophy is found proximal to these triangles.

The patient was treated with alternating courses of bismuth and oxophenarsine hydrochloride. At the end of sixteen months' treatment, the Wassermann reaction was still positive. At thirty months the Wassermann, Kline diagnostic and Kline exclusion reactions of the blood were still strongly positive. Three years later repeat serologic tests showed the Wassermann reaction to be negative and the Kline diagnostic and Kline exclusion reactions positive.

#### DISCUSSION

DR ROBERT C. JAMILSON, Detroit. After seeing the photographs of the original eruption, while I should not like to dispute the word of any one who has been taking care of the patient, I must admit that I have never seen an eruption of this type due to syphilis. Treatment might readily clear up an eruption of that kind. As far as the pigmentation is concerned, one finds a dyschromia from any kind of chronic inflammation.

DR ISAAC J. ARNSSON, Buffalo. Histologically, I think the picture is typical of syphilis.

DR DANIEL J. KINDEL, Cincinnati. It has been our good fortune in Cincinnati to hear Dr. Martinez, who gave a comprehensive story of pinta. In early pinta there are superficial lesions in the eruptive stage which disappear rapidly. Histologically the lesions in this case do not fit in with the active lesions of pinta as he described them. Diagnoses which I feel could be considered with more weight than pinta would be pellagra and, secondly, possibly an inflammatory process due to rubber gloves which causes depigmentation. On what was the diagnosis of pinta based?

DR GEORGE W BINKLEY, Cleveland I suggested the diagnosis of late dyschromic pinta of the skin for this patient in 1939, one year after antisyphilitic therapy was begun At this time it was too late to establish the causative spirochete in the twenty year old cutaneous lesion This demonstration would have been preponderant evidence in favor of pinta Since the patient lives in the United States, my colleagues have regarded the spirochete in this case as *Treponema pallidum*, but I believe that if this woman were a resident of Cuba, Mexico or South America, where many lesions of late pinta are seen, late cutaneous pinta would have been the diagnosis, for the following reasons In 1938, the involvement of the flexor surfaces of the forearms was of twenty years' duration On the flexor surfaces of the wrists were triangular areas of depigmentation, typical of pinta The lesions were mildly pruritic Complement fixation reactions and Kline reactions of the blood were strongly positive, and the histologic changes were consistent with those of late pinta One year later the erythroderma was almost gone There was a slow but continuous improvement from administration of oxophenarsine hydrochloride and bismuth At this time, six years after treatment was begun, there is only hyperpigmentation of the borders of the former erythroderma of the forearm A triangular area of permanent depigmentation remains on the flexor surfaces of the wrists I have seen a pintoid picture on the flexor surfaces of the forearms in North American Negroes with early syphilis, and I believe that *Treponema pallidum* can simulate pinta in some of its aspects Dr E P Liberthal has reported 3 cases of late or tertiary dyschromic pinta (*J A M A* 123 619 [Nov 6] 1943)

**Pyoderma Gangrenosum Associated with Non-specific Ulcerative Colitis** Presented by DR HAROLD N COLE and DR JAMES R DRIVER

M Y, a white woman aged 30, was presented before the Cleveland Dermatological Society on Feb 25, 1943 (*ARCH DERMAT & SYPH* 48 571-573 [Nov] 1943) with a diagnosis of amebiasis cutis She was hospitalized at Lakeside Hospital from January 6 to March 3, 1943 Numerous attempts were made to demonstrate amebas in the stools and in the mucosa by warm stage and zinc flotation preparations, but none were found Roentgenograms revealed ulcerative colitis of the transverse colon and sigmoid to the rectosigmoid junction The cecum was not involved

Treatment consisted of continuous use of moist antiseptic dressings of surgical solution of chlorinated soda and weak silver nitrate solution with benefit Zinc peroxide medicinal dressings were of no value After a combined course of emetine hydrochloride and chiniofon, the diarrhea subsided and the ulcers healed Sulfathiazole, previously tried, had been of no value

In September 1943 she was again hospitalized for three weeks, because of recurrent diarrhea and the appearance of more ulcers on her legs Healing of the ulcers occurred when the diarrhea was controlled by the administration of succinylsulfathiazole When use of this drug was discontinued, another exacerbation developed with more ulcers, and she was hospitalized for the third time, from Dec 18, 1943 to Jan 10, 1944 The drug was again administered, and healing of the ulcers occurred, together with relief from the colitis Since then she has continued to take the drug, without any further evidence of colitis or ulceration of the skin

The urine was normal The hemogram revealed a moderate degree of secondary anemia

DISCUSSION

DR HARTHER L KEIM, Detroit I agree with the diagnosis as suggested and feel that the lesion on the left calf still shows activity The honeycomb appearance of these lesions shows that I think that as soon as penicillin is available it should be used

DR ISAAC J ARNSSON, Buffalo Similar good results have been obtained from the use of tyrothricin

DR DANIEL J KINDEL, Cincinnati I have seen 3 cases, 1 presented at the medical meeting last November Tyrothricin was used at that time After I discounted my enthusiasm for the material, I finally had to say that it was of no value Another patient acquired the disease from another cause The disease in the third case followed internal tests and postage stamp grafting afterward In this woman a small nodule developed very rapidly The process was exceedingly rapid, in the course of twenty-four to forty-eight hours one could almost see the nodules move This blue undermined border also shows striae The organism is generally regarded as a microaerophilic type of *Streptococcus*

DR JAMES R DRIVER, Cleveland This patient was presented last year with a diagnosis of amebiasis cutis, partly because the ulcers resemble the ulcers of that disease and partly because of the fact that this patient's trouble started after she visited the Chicago World's Fair She has been in the hospital on three different occasions, and numerous attempts have been made to demonstrate amebas in the stools, but none have been found Her attacks are timed exactly with her attacks of colitis At that meeting Dr Netherton suggested that this case might fit into the group Dr Brunsting presented in 1930 I looked up this article and found that 5 cases were reported on at that time The photographs accompanying the article have convinced me that this case falls into that group In their cases they found that benefit was obtained by treating the patients for amebic dysentery At that time, of course, the sulfonamide preparations were not available, so I treated this patient on her first admission with emetine and she did improve somewhat The last two times that she was admitted I used succinylsulfathiazole Of course the dose is almost unlimited and can be kept up for any length of time This patient responded almost miraculously to this treatment She has had no trouble now for several months The diarrhea is kept under control by the drug, and the lesions are practically well She has had no exacerbations at all She takes a week or ten days' vacation from the drug, then starts it again, about 4 Gm a day The organism isolated in our case was a hemolytic staphylococcus

**Acrodermatitis Atrophicans Chronica with Fibrous Cutaneous Nodules** Presented by DR E W NETHERTON and DR W R HUBLER

C R, a white woman aged 61, was presented before the Cleveland Dermatological Society on Jan 28, 1943, with questioned diagnoses of acrodermatitis chronica atrophicans with fibrous nodules and mycosis fungoides (*ARCH DERMAT & SYPH* 48 126 [July] 1943)

The blood calcium level was 10 mg and the blood phosphorus level 3.9 Gm per hundred cubic centimeters

A section of a nodule removed for histologic examination showed a thin epidermis covered by a thin layer of hyperkeratosis Most of the interpapillary pegs had been obliterated by changes in the corium Throughout the corium there was a diffuse, and in places fairly dense, polymorphous cellular infiltrate The multiplicity

of cell types was striking. The infiltrate was composed of lymphocytes, large mononuclear cells, leukocytes, eosinophils, plasma cells, endothelial cells and connective tissue cells. There were pyknotic cells and some cellular debris in the delicate connective tissue stroma of the densely infiltrated areas.

The cutaneous nodules have decreased in size after seven low voltage roentgen ray treatments during the four months.

## DISCUSSION

DR HARTHER L. KEIM, Detroit. I do not think that this is acrodermatitis chronica atrophicans, the process has too many hypertrophic characteristics. The nodule definitely makes one think of mycosis fungoides.

DR MYER W. RUBINSTEIN, Pittsburgh. I believe that this case is typical and characteristic.

DR E. W. NETHERTON, Cleveland. One year ago we presented this case with a question regarding the possibility of mycosis fungoides. This was based on the histologic changes observed in a nodule which had been removed. I think that Dr. Keim's remarks are pertinent because of the changes observed in the tissue which was removed, and which showed multiplicity in type of cells in the infiltration. The changes are strongly in favor of the diagnosis of mycosis fungoides. At the previous presentation Dr. R. E. Barney discussed the case, and he felt that this possibility should be kept in mind. At that time he discussed the case he had observed, which was a case of acrodermatitis atrophicans vasculare terminating in lymphoblastoma. As for the sclerodermatous changes, these are seen in acrodermatitis atrophicans. This patient has the ulnar bands and the scleroderma-like changes on the legs which are sometimes seen in this disease.

#### A Case for Diagnosis (Lupus Vulgaris Erythematosus of Leloir?) Presented by DR. MAX E. KRAUSE for DR. HAROLD N. COLE and DR. JAMES R. DRIVER

M. M., a white man aged 48, was presented by Dr. J. R. Driver before the Chicago Dermatological Society in 1940, with a questioned diagnosis of lupus vulgaris erythematosus of Leloir (ARCH. DERMAT. & SYPH. 42: 199 [July] 1940).

The face is still involved by a grouped discrete brownish papulosquamous eruption especially prominent at the inner portion of the left eyebrow and over the forehead. There is a diffuse slightly raised moist grayish white proliferative involvement of the soft palate, tonsillar fossae, posterior pillars and a portion of the pharynx. There are also two small superficial nontender granular ulcers at the palatine junction. The patient's general health has remained good.

Treatment has consisted of cryotherapy, gold, acetarsone, bismarsen, chaulmoogra oil, radium bulb and electric cautery. Some improvement resulted from cryotherapy. Gold therapy was effective in causing remissions from time to time of the lesions on the face.

## DISCUSSION

DR. STANLEY CRAWFORD, Pittsburgh. I disagree with the diagnosis as presented. There is no appearance of lupus vulgaris to the eruption. The lesions of the eyebrows appear to be impetiginized.

DR. JAMES R. DRIVER, Cleveland. We took the patient to a meeting of the Chicago Dermatological Society about four years ago and there was a good deal of discussion as to whether the disease was lupus erythematosus or mycosis fungoides. The histologic picture favored

lupus erythematosus, but several of the dermatologists present believed that the clinical picture was in favor of lupus vulgaris. One favored a diagnosis of true tuberculosis in this case. It has been a chronic process and has responded best to cryotherapy. It has been difficult to influence with any kind of treatment.

#### Lupus Erythematosus Hypertrophicus Presented by DR. DONALD N. MACVICAR for DR. HAROLD N. COLE and DR. JAMES R. DRIVER

M. K., a white woman aged 28, complains of an eruption of the face. She states that when she was 6 years old an eruption developed on the legs, later spreading to the arms and face. In a period of several months the arms and legs became clear, but the process on the face has persisted. At times the areas of the face are pruritic.

Aside from the usual infections of the upper respiratory tract, the patient's health has been excellent. She states that she sunburns readily and that excessive exposure to the sun results in an exacerbation of the eruption. There is no family history of tuberculosis.

On the bulbous portion of the nose and over the lips are flat raised firm confluent lesions, varying from 3 to 10 mm. in diameter. The surface of these lesions is rough and hypertrophic, with some areas of exudation and crusting. Similar lesions are present on the prominence of the right cheek and below the right eye. There are some small red and brown papular and follicular lesions scattered over the dorsa of the hands and wrists.

Histologic examination of a piece of skin removed from one of the lesions on the side of the nose revealed a well developed horny and granular layer of the epidermis. There were a few cells in the mucosal and basal layers with vacuolation of the cytoplasm and distortion of the nuclei. In the upper portion of the corium a moderate degree of edema was present, and numerous dilated blood vessels were seen. Some perivascular small round cell infiltration and several focal accumulations of small round cells and epithelioid cells were found in the same area. There were numerous large sebaceous glands throughout the entire section, and several keratotic follicular plugs were present.

Prolonged therapy with injections of gold sodium thiosulfate and various bismuth preparations, together with the local applications of solid carbon dioxide, has produced little improvement. There have been frequent periods of exacerbation with intervals of remission.

## DISCUSSION

DR. ISAAC J. ARNSSON, Buffalo. Were tests for porphyrinuria made for this patient? Clinically, the eruption suggests hydroa aestivale.

DR. JAMES R. DRIVER, Cleveland. I think that I am correct in stating that this test was not made. Lesions were present in the winter as well as in the summer.

DR. ISAAC J. ARNSSON, Buffalo. The patient claims seasonal improvement. The hypertrophic lesions may be due to scarring.

DR. HAROLD N. COLE, Cleveland. The histologic appearance of this eruption is typical of lupus erythematosus, with the plugging and cellular infiltration around the hair follicles.

DR. E. W. NETHERTON, Cleveland. I believe, considering the type of lesions and the absence of scarring, that the disease is not hydroa aestivale. In most of the cases one will find that the scarring covers most of the exposed parts of the face instead of being patchy.

**Dystrophia Mediana Canaliformis** Presented by  
DR MAX E KRAUSE for DR HAROLD N COLE and  
DR JAMES R DRIVER

D K, a white woman aged 41, complains of a deformity of the left great toe nail. The nail was normal until three years ago, when there began to develop a median longitudinal deformity with a bluish discoloration as if traversed by a blood vessel. Recently, the bluish discoloration disappeared and desquamation occurred. There are no subjective symptoms or history of previous injury to the nail.

The abnormality of the left great toe nail consists of a 3 mm wide centrally located longitudinal furrow or groove extending from the base to the free edge. The groove is filled with soft cornified nail debris. The nail fold, bed and matrix appear normal. All other nails are normal.

**Dystrophia Mediana Canaliformis** Presented by  
DR MAX E KRAUSE for DR HAROLD N COLE and  
DR JAMES R DRIVER

J B, a white man aged 54, was told that at 1 year of age he had an infection of the third finger of the left hand with a subsequent loss of its nail. With regrowth of the nail a median longitudinal deformity appeared which has persisted unchanged. The deformity is asymptomatic.

The patient exhibits a central longitudinal deformity of the nail of the third left finger. It consists of a ridge that seems to originate in the nail fold and extend outward, forming a shallow furrow or groove within the nail plate. The other nails are normal in appearance. There are no cutaneous defects or other abnormalities.

#### DISCUSSION OF TWO PRECEDING CASES

DR C K HAISLEY, Detroit. I have seen a good many such lesions on finger nails. In fact, I have one on one of my own finger nails. It resulted from handling too much radium without using enough caution. I have also seen them on radiologists who remove foreign bodies.

DR RALPH R DUCASSE, Cincinnati. I also wonder whether in the use of radium the contact with the radium was actually made or whether it was from a long distance exposure.

DR C K HAISLEY, Detroit. That is hard to tell. Frequently one has to use the fingers when in a hurry.

DR JAMES R DRIVER, Cleveland. The question is whether this condition is a nevus or whether it is due to trauma. The case of D K seems to be an instance of the second type, however, the patient (41 years old) has had the condition for only a year and gives no history of trauma. Similar changes can be seen in persons who have had too much radiation, particularly in physicians and technicians who use roentgen rays and radium, and yet the affected areas do not look exactly like this one. The growth will separate after it has extended about the median line of the nail, and then the process starts again as the nail grows out. In the case of the man who has had it since infancy, he was told that he had had some sort of infection and he has had this process ever since. In the case of D K, trauma is probably the causative factor. Clinically, the two lesions look different.

DR B F BARNEY, Columbus, Ohio. In the case of the man, I think that one is dealing with trauma, a growth from the nail bed. Owing to insufficient blood supply, the nail separates as it grows out. Regarding the case of the woman there is a lesion which seems

to be an actual tube of cells which erupts, then the process starts all over again. I agree with the diagnosis for the woman and disagree with the diagnosis for the man.

**Congenital Ectodermal Defect** Presented by DR  
DON R PRINTZ and DR SAM AYRES III

H K, a white man aged 27, presented from the department of dermatology and syphilology, Cleveland City Hospital, service of Dr Harold N Cole and Dr James R Driver, has the complaint of being unable to tolerate heat. He cannot remember ever sweating and has always had a sparsity of hair on his body. There is no family history of similar disturbances or epilepsy. He is married and has one normal son.

The skin on the entire body is soft and of fine texture with absence of moisture on palms and soles. On the face, especially around the eyes, mouth and sides of the neck, are many yellowish brown papules about 1 to 2 mm in diameter which tend to be arranged in a linear fashion. The eyes are normal. The nose is small, with a depressed bridge covered with atrophic skin and lined with an atrophic mucous membrane. The lips are thick and dry. The only erupted teeth are two lateral incisors and two canine teeth in the upper jaw and two in the lower jaw. The hair on the scalp and chest and in the axillas is lanugo-like, that on the face is normal, except for an area of alopecia over the right mandible. There is no pubic hair. The nails are normal.

The hemogram and urine were normal. The blood chemistry was normal. The Wassermann reaction of the blood was negative on nine occasions, while the reaction to a Kline diagnostic test varied from negative to strongly positive. The spinal fluid was normal. Roentgenographic examination of the chest showed normal conditions and of the tibia showed no evidence of periostitis.

Histologic examination of a section of skin taken from an axilla showed mild hyperkeratosis, keratotic plugs in dilated follicular orifices and intracellular edema of the epidermis. The hair follicles and sebaceous gland were normal. A specimen taken from the skin of the neck showed moderate hyperkeratosis, a small area of parakeratosis and mild intracellular edema of the epidermis. There were a few small hair follicles present. The follicular orifices were dilated and filled with keratotic plugs. Some sebaceous glands were normal, while others were disorganized. No sweat glands were found. The epidermal layer was invaginated at places to form relatively large cystic spaces filled with keratotic material.

#### DISCUSSION

DR ROY L KILE, Cincinnati. In this case I am in favor of a diagnosis of poikiloderma atrophicum vasculare. Inasmuch as the nails are normal, the hair is normal and there is definite atrophy and telangiectasia, I believe that this is the most likely diagnosis.

DR HOWARD J PARKHURST, Toledo, Ohio. I felt that this case is a good instance of congenital ectodermal dysplasia as described by Goeckerman.

DR HAROLD N COLE, Cleveland. In my opinion, as we more carefully analyze the ectodermal dysplasias, we are going to find more and more varied manifestations of this unusual condition. In one case it may be a more extensive involvement of the skin, in another the teeth, in another perhaps the eyes, etc. Moreover, it may well be that we shall gradually recognize all variations from a complete ectodermal dysplasia such as first described by Clauston (Clauston, H R. The

Major Forms of Hereditary Ectodermal Dysplasia [with an Autopsy on the Anhidrotic Type], *Canad M A J* 40 1-7, 1939) down to the individual with but a few unusual involvements that will test our powers of observation and analysis to place them properly. And, too, we may find occasionally types involving not only ectodermal structures, but also mesodermal tissue, that is, bone.

**Trichophytosis Barbae** Presented by DR E W NETHERTON and DR W R HUBLER

R K, a white farmer aged 37, was first seen in the Cleveland Clinic Foundation Hospital on April 28, 1944. He noticed three small round red papules on the left side of his neck, two months ago. These increased in size rapidly, each one reaching the size of a silver dollar in about five days. The surface of each of these superficial lesions appeared as a series of raised red concentric rings. These disappeared in about two weeks with applications of an "eczema salve," leaving three or four small papules and dark red macules, where the lesions had been. At this time, two new lesions appeared on the upper lip. These grew slowly into crusted exuding nodules which persisted about a month and then disappeared, leaving erythematous areas. During this time, the patient received biweekly injections of a calcium preparation and soothing local applications. Four weeks ago, several new lesions appeared on the lower lip and chin. These have developed slowly to their present extent.

The patient disposed of a bull four months ago. This bull had a swollen jaw, which was discharging pus from several openings.

There are three closely adjacent crusted raised indurated nodular lesions, each about the size of a silver dime, on the left side of the lower lip. These are surrounded by erythematous areolas and are exuding a purulent discharge. Similar lesions are present on the right side of the chin and in the submental region. A few small pustules are seen in all the lesions. Several smooth or scaly firm red nodules and papules are scattered over the bearded area of the face and neck. Most of the hairs in all involved areas are easily removed. There are two purplish erythematous macules involving most of the upper lip.

Microscopic examination of a potassium hydroxide preparation of hairs from the involved areas showed innumerable small spores and hyphae, located in and surrounding the hair shafts.

The Wassermann and Kahn reactions of the blood were negative. The blood sugar level and the hemogram were normal.

DISCUSSION

DR STANLEY CRAWFORD, Pittsburgh: This disease could be considered actinomycosis. Has search been made for yellow bodies? One could still consider an uncomplicated sycosis.

DR ROY L. KILF, Cincinnati: At times tinea barbae is rather difficult to cure. This is contrary to the ease with which fungous infections of the scalp are usually cured by local therapy in the Middle West. Many years ago Dr M. F. Engman Sr reported on the intravenous injection of typhoid vaccine in cases in which the disease is resistant to local therapy. The results were apparently favorable.

DR HOWARD J. PARKHURST, Toledo, Ohio: I have seen an occasional instance of this type. All the patients have been farmers. In all the disease has been due to the bovine type of organisms, and all have responded well to applications of diluted iodine.

DR E. W. NETHERTON, Cleveland: This case presents one feature which is thought to be common in sycosis barbae, namely, that the upper lips are seldom involved. This patient did have a superficial erythematous scaly lesion on the upper lip at the onset of the eruption, but this has cleared up. Against the diagnosis of actinomycosis is the fact that the lesions are not as deep as those of actinomycosis, the surfaces of the lesions in this case are crusted, and there are numerous follicular pustules on the lesions. The demonstration of the presence of the spores and hyphae in and about the hair and the absence of granules in the exudate were considered sufficient to rule out the possibility of actinomycosis.

**Angioendothelioma of the Skin** Presented by DR E W NETHERTON and DR W R HUBLER

J F, a married man aged 52, came to the Cleveland Clinic Foundation Hospital on July 12, 1940, because of an eruption on the feet of six months' duration. His past and family histories were noncontributory. The eruption started with desquamation between and beneath the toes. Four months later the dorsal surface of the feet became red and edematous, and a purulent exudate developed between the toes.

When he first came to the clinic, there was a moderate amount of dry scaling between and beneath the toes. There were no fissures in the interdigital spaces. However, between the second and third toes of the left foot, there was a small ulcer. The patient stated that recently he had removed a small "corn" from this interdigital space. There were slight edema of the lower portion of the legs and a poorly demarcated subacute erythematous edematous scaly dermatitis on the dorsal surface of each foot. Hyphae were not found in potassium hydroxide preparations of material removed from interdigital spaces.

After rest in bed, magnesium sulfate soaks and application of a mild tar ointment, the eruption disappeared. He remained free of the eruption until early in 1943. In December 1943 he was admitted to the hospital, because of partial cardiac decompensation. At this time there was a polymorphous eruption involving the feet, the lower portions of the legs and the knees and hands. There were fairly well demarcated, light red gyrate scaly plaques on the soles, the dorsal and lateral surfaces of the feet and the inner surfaces of the ankles and lower portion of each leg. The scales were large, gray, dry and adherent. The epidermis was thin and slightly atrophic. There was no induration.

There was a poorly circumscribed soft brownish pink smooth plaque the size of a half-dollar just above the right knee.

There was a similar but smaller lesion near the left knee. The lesion on the left knee was removed for histologic examination.

The third type of lesion was located on the dorsal and lateral surface of the right fifth finger, the adjacent area of the dorsal surface of the hand and the lateral surface of the right ring finger. This lesion was a brownish red smooth well demarcated indurated plaque. After the removal of a biopsy specimen from this plaque, the lesion showed decided involution. A similar but smaller indurated nodule was present on the lateral surface of the left ring finger. Four treatments of 75 r of unfiltered roentgen rays have been given to these lesions on the hands and feet. The induration of the lesions on the hand has almost disappeared, and the plaques on the feet and legs are not as erythematous as before. However, the chief characteristics of the eruption have not changed.



Tissue was removed from the plaques on the right hand and the left knee and an erythematous scaly plaque on the inner surface of the left leg for histologic study. The section from the edematous plaque showed an inflammatory reaction of the corium and subcutaneous tissue. The epidermis was covered with a layer of hyperkeratosis but was otherwise normal. Throughout the corium there were areas of perivascular infiltration, composed of lymphocytes, large mononuclear cells and an occasional neutrophilic leukocyte. Many of the vessels were dilated. The cellular infiltrate in the subcutaneous fat included lymphocytes, fibroblasts and phagocytes containing a golden brown pigment.

A section from the hand showed a thick layer of hyperkeratosis, but otherwise the epidermis was normal. There was a diffuse cellular infiltration of lymphocytes and large mononuclear cells throughout the corium with a richly cellular proliferation of the connective tissue, and in the upper portion of the corium there were many irregular clear epithelium-lined spaces. There were also clear spaces without definite cellular lining, which could be interpreted as artefacts.

Tissue from the lesion near the left ankle showed atrophic epidermis covered with a thick layer of hyperkeratosis. The granular layer was patchy and indistinct. The rete mucosum was thin, and the cells stained poorly. The basal layer was intact. The interpapillary pegs were obliterated. In the papillary layer and upper portion of the corium there was a vascular network of sinusoidal character surrounded by polygonal, oval and fusiform endothelial cells, some in mitosis.

Dr Harry Goldblatt made a histologic diagnosis of subacute inflammation of dermis and subcutaneous tissue in the lesion removed from the hand and knee, but he considered the lesions of the leg as angioendothelioma of the skin, probably arising from vascular hamartoma.

An intradermal tuberculin test (purified protein derivative) elicited a positive reaction. The Wassermann and Kahn reactions of the blood were negative. The hemogram and urine were normal.

#### DISCUSSION

Dr ISAAC J ARNSSON, Buffalo. I think that multiple diopathic hemorrhagic sarcoma should be considered. Histologically, there are elements which speak for it. There are a number of blood vessels and sarcoma-like invasion of the cutis.

Dr E W NETHERTON, Cleveland. We seriously considered the diagnosis of sarcoma of Kaposi in this case, but because of the lack of hemorrhages and pigmentation this diagnosis was ruled out. Dr Goldblatt's opinion is that although there are some features which favor the diagnosis of Kaposi's sarcoma, in the final analysis the histologic observations rule out this possibility. The diagnosis with which this patient was presented is a pathologic one. The angioendotheliomatous change is striking in the sections of the tissue taken from the lower portion of the leg.

**Scleroderma en Coup de Sabre** Presented by Dr DONALD N MACVICAR for Dr HAROLD N COLE and Dr JAMES R DRIVER

M F, a white boy aged 13, complains of a lesion of the scalp of three years' duration. The lesion started as a small spot on the right side of the forehead and has gradually extended back over the scalp. Some pruritus in the area has been noted at times. He can remember no trauma in the region of involvement.

On the right side of the scalp, extending from the hair line above the region of the right eye backward

over the head, is a bald linear lesion, 6 by 12 cm in size. The skin of the area is of an ivory color and is bound firmly to the underlying skull. The border of the lesion has a delicate pink color. The entire area is depressed below the surface of the scalp into an underlying furrow in the skull.

Thyroid extract was prescribed and a soothing ointment applied locally. Since the inception of therapy the lesion has increased slightly in size.

#### DISCUSSION

Dr HARTHER L KEIM, Detroit. I have seen this disease before, and I remember that in both cases it progressed down over the face. I thought that the alopecia resembled pseudopelade. There are slight itching and slight scaling suggestive of alopecia. The disease appears to be located in the central part of the scalp and has made a definite furrow into the skull.

Dr HAROLD N COLE, Cleveland. It would be unusual to see pseudopelade limited to one area on the skull. Usually the lesions are found freely distributed. Moreover, this lesion is more or less linear in type. These cases of saber cut scleroderma may involve the scalp alone, the forehead alone, or both combined. The picture presented here with the involvement of the bone would support the diagnosis of scleroderma en coup de sabre.

**Mycosis Fungoides** Presented by Dr B LEVINE

C N, is a white woman aged 37. Her mother died fifteen years ago during menopause. Her father, three sisters and two brothers are living and well. No brothers or sisters died. There is no history of tuberculosis or malignant neoplasms in the family.

She had an appendectomy eighteen years ago and a thyroidectomy fifteen years ago for a toxic goiter. There is no history of eczema, psoriasis or other eruption prior to the present illness. She was delivered of a normal child two years ago. The patient believes that she is pregnant at present.

The present illness began three years ago with an eruption on the body. This did not itch at first, but itching started when she became pregnant. The eruption did not get worse during the course of the pregnancy, but after the birth of the child the lesions became more numerous, pruritic, scaly and thickened, with some tumor formation. The eruption then spread over the face, neck and limbs as well as the body and thighs. These were large confluent plaques, dark red, thickened, infiltrated and scaly and circinate and gyrate in shape, leaving areas of normal skin between. Some of these plaques were somewhat elevated. Many of them, especially on the face and upper part of the body, are regressing from roentgen ray therapy the patient received at the Mayo Clinic. A tumor mass 2.5 cm high on the neck has cleared up with roentgen ray therapy.

The Kline slide precipitation reaction was negative throughout. The urine was normal. The hemogram is as follows: red blood cell count, 3,810,000, white blood cell count, 6,850, hemoglobin content, 75 per cent, polymorphonuclear neutrophils, 69 per cent, lymphocytes, 14 per cent, monocytes, 12 per cent, and eosinophils, 5 per cent. The red blood cells and platelets appear normal.

A section of the skin revealed that the epidermis was thicker than average. Interpapillary projections were larger than average, coarse and blunt. In the upper portion of the dermis just beneath the surface epithelium and in the papillary projection there was considerable round cell infiltration composed of lymphocytes, monocytes and plasma cells. There was an increase in the

number of fibroblasts and capillaries in this section. No giant cells were seen. The cellular infiltrations were most evident in perivascular locations but diffusely involved the entire upper part of the dermis. No areas of necrosis were present. The deeper layers of the epidermis showed no appreciable cellular infiltration except in the stroma immediately about sebaceous glands and hair follicles, where there was slight fibroblastic proliferation and infiltration by wandering cells similar to those which richly infiltrate the upper portions of the dermis.

## DISCUSSION

DR STANLEY CRAWFORD, Pittsburgh. I am of the opinion that roentgen ray therapy is the only efficient treatment. The ultimate outlook is hopeless. To keep the lesions under control, one may as well treat them with roentgen rays. The question in each case is how many units of roentgen ray should be given.

DR FREDERICK M. JACOB, Pittsburgh. For a matter of five years my colleagues and I have been using roentgen rays and chaulmoogra oil when tumors occur. We have never decided whether chaulmoogra oil does any good, but I am giving it a fair trial.

DR B. LEVINE, Cleveland. The diagnosis, both clinically and microscopically, is obvious. I have treated the upper part of the body with filtered roentgen rays. The rest was left untreated so that some unaltered lesions would remain for this meeting.

#### Systematized Epithelial Nevus Presented by DR JOHN A. GAMMEL

Mrs. R. C., a white woman aged 28, has two healthy children, 4 and 5 years old. When the patient was 6 weeks old, a "baby rash" was noticed, which persisted and gradually spread. It has now been stationary for many years. Three years ago, after the tops of some of the lesions had been scraped off, a vesicular outbreak occurred which lasted for several weeks and caused great discomfort. There are no subjective symptoms. The patient enjoys good health.

The eruption is almost generalized and is roughly symmetric. The face is clear, except for some rough spots at the side of the nose. The skin in general is dry, and the upper part of the back shows a large area studded with punctate keratoses.

The outstanding lesions are in the folds of the extremities—the anterior and posterior axillary folds, the cubital fossae and in the popliteal spaces. The disease is most evident in the right groin. In these areas there are linear lesions made up of more or less elevated, and in places verrucous, efflorescences. The softer lesions are of skin color, and the larger and more elevated ones light to dark brown.

Confluent lesions extend in streaks from the lateral aspect of the right wrist to the palm, where they fan out and become hard and wartlike. Here the color shows a yellow hue. The eruption is to a lesser degree present on the left hand. A heavy streak extends from the right ankle to the big toe. There are lesions on both insteps.

The stratum corneum was thick and contained a few widely spaced pillars of parakeratosis. The lower surface of the horny layer projected into sella turcica-shaped valleys, formed by a wavy epidermis.

The main disturbance in the tissue was in the basal layer. The basal cells had a low cuboidal shape, and there was intracellular edema in many. Above these low cells the rete cells showed an amorphous degeneration. These areas were more eosinophilic than the

normal rete Malpighii. In places the full thickness of the rete showed eosinophilic degeneration of the squamous cells. More severely involved areas of the epidermis were fragmented.

## DISCUSSION

DR E. W. NETHERTON, Cleveland. I should like to suggest the diagnosis of ichthyosis hystrix.

DR HOWARD J. PARKHURST, Cleveland. I should like to know why these cases should be classified as ones of ichthyosis hystrix when the intervening skin is normal and shows no evidence of ichthyosis.

DR E. W. NETHERTON, Cleveland. I do not believe that one always has to have ichthyosis of the ordinary type associated with history of ichthyosis.

DR JOHN A. GAMMEL, Cleveland. I thought that this patient's case closely resembled the cases reported by Dr. Morris Waisman and Dr. Hamilton Montgomery (*ARCH. DERMAT. & SYPH.* 45:259-282 [Feb.] 1942). The histologic picture concurs with their description.

#### Xeroderma Pigmentosum with Precocious Malignancy Presented by DR E. W. NETHERTON and DR W. R. HUBLER

L. K., a boy aged 3½ years, presents an eruption which began when he was 19 months of age. The family history shows no consanguinity of the parents. There are three sisters, who are well. There has been no similar eruption in the family or either parent.

The mother states that when this child was 19 months of age "freckles" began to develop on the face. The child played in the sunshine without any protection. During the past year numerous small hyperpigmented spots have developed on the face, neck and exposed portions of the chest and arms. Likewise, small hyperkeratotic papules, filiform warts and crusted lesions have developed. Some of the crusted lesions have healed, leaving pinkish white scars. Five weeks ago, a tumor appeared on the left ala of the nose. The lesion has grown rapidly and has become covered with an adherent hemorrhagic crust. More recently, smaller crusted lesions have appeared below the right eye.

There is an eruption limited to face, neck, upper portion of chest, arms and exposed portions of the legs. It consists of numerous small pigmentations, small keratotic papules and filiform keratoses and scattered pink scars. There are a few telangiectases on the scarred areas. There is a large nodule on the left side of the nose. This involves the nasolabial fold and is covered with an adherent hemorrhagic crust. There are irregular crusted areas on the right side of the face.

## DISCUSSION

DR HARLEY A. HAYNES JR., Akron, Ohio. I think that this is a typical case and unusual in both the severity and the precocity of the epithelioma. In 1936 I reported a case of xeroderma pigmentosum with multiple malignant lesions in a boy 3 years and 10 months old. At that time this patient was the youngest of which I could find record.

DR HAROLD N. COLE, Cleveland. I have had a case of this type—that of a girl who was about 1½ years old when I first saw her and who is now 27. She has been treated for at least forty to fifty epitheliomas of the face and hands. She keeps out of the light except mornings or evenings and always wears a hat with a red lining. She uses 10 per cent phenyl salicylate in yellow petrolatum, which acts as a protection against ultraviolet radiation.



DR FREDRICK M JACOB, Pittsburgh The mother says that a good many of the epitheliomas rub off of their own accord I have removed about five from a girl at home There is skin grafted on almost the entire forehead The grafted skin looks normal, and xeroderma pigmentosum does not seem to have developed in it

DR ROBERT C JAMIESON, Detroit The mother mentioned, on questioning, that this boy is one of four and the only one to have the lesions In his early life he was rather sickly and was exposed almost constantly to the sun I wonder whether this disease is a result of exposure to the sun or ultraviolet rays

DR MYER W RUBENSTEIN, Pittsburgh I do not think so In this particular instance, it is interesting to note that there are no lesions on the lower extremities at all With reference to the use of radiation The boy had several lesions on the back of his neck, and they dropped off spontaneously, hence I do not give too much credit to roentgen rays I think that the boy's outlook will be best if he will keep himself absolutely out of the sunlight However, this can be done, as he can sleep in the day and work at night

#### Adenoma Sebaceum (Pringle Type *Forme Fruste*)

Presented by DR DONALD N MACVICAR, for DR HAROLD N COLE and DR JAMES R DRIVER

J C, a white boy aged 7 months, was seen because of several growths on the toes When he was 3 days old, a small swelling was noted on the left middle toe This lesion persisted and increased slowly in size A similar swelling developed on the right middle toe and has slowly increased in size Mental and physical development have been normal There is no family history of cutaneous disease or epilepsy

The child seems alert and is of normal physical development, except for the toes There is a firm raised dull red tumor involving the dorsum and medial surface of the left middle toe Similar, but smaller, lesions are present on the right middle and right second digits The skin of the face is normal

Roentgenograms of the feet revealed no abnormality of the bony structure

Histologic examination of a piece of tissue removed from one of the lesions revealed a moderate degree of parakeratosis of the epidermis The granular layer was well developed The rest of the epithelium was normal The tissue beneath the epidermis consisted of interlacing bundles and strands of loose fibrous tissue Many nuclei were present, and some of the cells presented a vacuolated, almost foamy, appearance of the cytoplasm

#### DISCUSSION

DR HARLEY A HAYNES JR, Akron, Ohio I disagree with the diagnosis of adenoma sebaceum because I believe that neither the clinical picture nor the histologic structure points to that I am not ready to offer another diagnosis, except that of a congenital defect

DR HOWARD J PARKHURST, Toledo, Ohio In the disease described by Pringle, I believe, the adenoma sebaceum on the face was accompanied with subungual fibromas It would be interesting to follow this case to see whether an adenoma sebaceum develops on the face

DR HAROLD N COLE, Cleveland The baby presents these unusual subungual growths on the toes—histologically fibromas in type There are no lesions on the rest of the skin The child is thus far perfectly alert and apparently normal Nevertheless, I am not aware

of any congenital defect producing this picture A forme fruste of Pringle's adenoma sebaceum seems to be the best explanation As Dr Parkhurst says, we are going to follow this baby There may be mental deficiencies later It is a remarkable case in my estimation

#### A Case for Diagnosis (*Periarteritis Nodosa?*)

Presented by DR DON R PRINZ and DR SAM AARFS III

J F, a white man aged 69, complains of a generalized eruption of three years' duration characterized by exacerbations and remissions The present episode started nine months ago with low grade fever, general malaise, loss of weight and generalized muscular tenderness The lesions have been pruritic in recent months The patient gives no history of allergy or ingestion of drugs His general health in the past has been good

He presents a generalized eruption which is papular to nodular in character, the lesions average about 0.5 cm in diameter The primary lesion is an erythematous papule which extends into the subcutaneous tissue and acquires a yellow pustular appearance However, repeated lancing of the papules reveals no purulent content, only a thin serous material and bright red blood The papules regress, leaving a light brownish pigmented area Similar lesions have appeared on the buccal mucosa and pharynx The lymph nodes are not abnormal There are discrete freely movable nodules on the arms and abdomen The liver is palpable about 2 fingerbreadths below the right costal margin The heart is not enlarged, but a systolic murmur is present over the entire precordium Blood pressure is 110 systolic and 50 diastolic There are rales in the bases of both pulmonary fields and slight pitting edema of both legs, more pronounced in the right

The urine was normal The hemogram revealed 6 Gm of hemoglobin per hundred cubic centimeters of blood, 1,640,000 erythrocytes and 4,150 leukocytes, with 2 per cent eosinophils, 66 per cent polymorphonuclear neutrophils, 20 per cent lymphocytes, 4 per cent monocytes and 8 per cent unknown Studies of smears showed the bone marrow to be normal Aerobic and anaerobic cultures of blood, cutaneous lesion and bone marrow were negative for bacteria and fungi A typical cutaneous lesion processed and injected into a guinea pig gave no evidence of disease at autopsy Results of determinations of concentrations of bromides and iodides in the blood and urine were within normal limits Chemical examination of the blood revealed 130 mg of sugar, 118 mg of cholesterol and 147 mg of urea nitrogen per hundred cubic centimeters of blood The sedimentation rate was rapid Total protein was 6.3 Gm, albumin 3.5 Gm and globulin 2.8 Gm Kline reactions of the blood for syphilis were normal Roentgenograms of the lungs and heart showed no parenchymal involvement of the lungs However, there was an abnormal prominence at the right hilus which was probably due to blood vessels rather than to lymph nodes The intradermal tuberculin test with purified protein derivative (dilution 2) revealed 2 cm of induration in forty-eight hours The results of agglutination tests for Brucella, Proteus X<sub>19</sub> and typhoid and paratyphoid A and B organisms have been negative

Microscopic examination of a typical cutaneous lesion revealed a normal epidermal layer with no hyperkeratosis The papillary layers and superficial corium were edematous In the superficial portion of the corium and extending deeply in a perivascular distribution was an inflammatory reaction which was characterized by edema and an infiltration of polymorphonuclear cells and lymphocytes The cellular exudate showed necrosis

with fragmentation of fibroblasts forming large stellate cells which were occasionally in whorls grouped around capillary spaces. Histologic examination of a subcutaneous nodule from the right forearm showed a collection of fat with little supporting tissue and vessels. A section of bone marrow was about 95 per cent hemopoietic material and the remainder fat. A normal distribution of cells was seen with the usual predominance of myeloid elements. A smear of bone marrow showed a normal cytologic picture with an occasional blast form but not in sufficient numbers to indicate a pathologic process.

Treatment has consisted of repeated transfusions of whole blood and a thorough trial of sodium salicylate and sulfathiazole. There has been no change in the patient's general condition or cutaneous manifestations.

## DISCUSSION

DR HERBERT H BAUCKUS, Buffalo. There are a variety of lesions on this man, therefore I think that the diagnosis is open to question. On the left side of the trunk I felt two distinct nodules in the skin, and I suspect the picture of Hodgkin's disease might appear.

DR LOREN W SHAFFER, Detroit. There are unusual features in this case. The picture is that of an apparent background of toxemia and severe anemia, which would go with a toxic eruption. I should not expect to find the blood picture which the patient has in a person with Hodgkin's disease. By saying the "blood picture," I mean the anemia more than the differential count.

DR HAROLD N COLE, Cleveland. This patient has been under observation off and on for the last three or four years, and he has at various times been hospitalized because of the severity of his disease. He has had many transfusions. At no time have blood cultures been positive. At no time has the blood picture suggested lymphoblastoma. Lymph nodes have been taken out and sternal punctures made, but we have been unable to arrive at the diagnosis of lymphoblastoma. On the other hand, we are dealing with a systemic process which comes and goes. The temperature changes suggest Hodgkin's disease. He will get better and go along for a while and will then come back again looking and feeling much the same as he is now. Many of the tumors are subcutaneous and will come up to the surface and will break, and he will scratch them open. After studying the whole situation we did not think of any disease that would fit into this picture other than periarthritis nodosa. As everybody can see now, he is a sick man. He is seriously anemic, and unless more transfusions are given to him he may not live long. He probably has the same sort of nodules in the internal organs.

## CLEVELAND DERMATOLOGICAL SOCIETY

JAMES R DRIVER, M.D., *President*

GEORGE W BINKLEY, M.D. *Secretary and Reporter*

May 25, 1944

## Herpes Simplex Resembling Herpes Zoster Presented by DR BENJAMIN LEVINE

D H is a white woman aged 31. Her mother is living and well but her father died of tuberculosis. Two brothers are living and well but one sister died of tuberculosis.

At the age of 7 years she had a severe attack of influenza. After the attack of influenza, "cold sores" developed. They recurred always in the same locations, either on the right side of the nose or on the right cheek. Sometimes an attack would be precipitated by excessive exposure to the sun and on other occasions would appear for no apparent reason. Since she was 7 years old, she has had almost two score attacks of herpes. The last attack, which began on May 17, 1944, was ushered in with localized pain, generalized malaise and some febrile reaction. It is by far the severest and the most extensive eruption which she has had. The patient complains of burning and smarting of both eyes, and yet there are no visible lesions. Examination shows lesions on the anterior and right side of the nose and the right malar region. There are numerous groups of vesicles that are almost confluent. There are several little groups of vesicles in the right malar region laterally and in the central part of the forehead.

Treatment has consisted of intravenous injection of 10 cc of 10 per cent aqueous solution of sodium iodide on May 20 and May 24. She refused serial vaccinations with cowpox vaccine.

## DISCUSSION

DR JOHN A GAMMEL. I think that the history of frequent recurrences rules out herpes zoster. The attacks come on about every six months or so, and this frequency is common with herpes simplex. I suggest therapeutic smallpox vaccine or moccasin venom. I have had fair success with both of them.

DR BENJAMIN LEVINE. I saw this patient for the first time four or five days ago. The lesions looked like typical herpes zoster, with the close grouping of the vesicles and the wide extent of the lesions and their distribution. The lesions slightly overlapped the midline in the same way that the nerve fibers overlap. Also their keeping completely to one side of the face suggested herpes zoster. Because of the history, however, I called the disease herpes simplex instead of herpes zoster. It presented that particular problem of diagnosis.

DR HUGO HECHT. This is an unusual case. Herpes simplex seldom presents more than fifteen or twenty small vesicles, all at the same time and all of the same size. Rarely more than 20. I do not see why herpes zoster could not be considered. I think that there must be an irritation in the center of the nerve. It is always located in the same place, on the right side of the face, hence the maxillary nerve which is involved. I think that it would be interesting to send the patient to a neurologist to see whether there is something wrong. I think that the disease is herpes zoster and not herpes simplex. The two diseases are related, as both are caused by a virus. Herpes zoster is an infection of the ends of the nerves.

DR BENJAMIN LEVINE. The lesions in previous attacks have been more like those of herpes simplex—sharply defined and limited. On this occasion the lesion looked like one of herpes zoster. Previously the disease may have been nothing but herpes simplex, but on this occasion it was herpes zoster.

## Folliculitis Keloidalis Presented by DR BENJAMIN LEVINE

L S, a Negro aged 32, is a service station attendant. He had stomach trouble as a child and has recently been discharged from the Army because of gastric ulcers. He acquired syphilis in 1929. The serologic reaction was negative when he entered the Army in November 1942.

In 1935 pimples appeared on the back of the neck and have persisted. Eventually a large part of the scalp was involved. The occipital portion of the scalp and the nape of the neck are studded with numerous pinhead to split pea-sized tumors of keloidal type, which are smooth and shiny. The occipitoparietal regions are covered with a dark chamois-colored tumor mass that is confluent and ridged longitudinally. There were some pruritus and soreness. The Kline exclusion reaction was negative.

Histologic study revealed granulation tissue in the dermis and subcutaneous areas. There were scattered giant cells and some structures suggesting degenerated hairs in the granulation tissue. In two sections the granulation tissue lined a small defect. At some distance from the cellulitis and sinus, there were scarring and round cell infiltration about cutaneous glands and hair follicles. In the region of the former the epidermis was elevated. There was abundant brown pigment in the basal layer of the epidermis.

The treatment consisted of roentgen radiation to the occiput, four doses of 100 r each, filtered through 1 mm of aluminum.

#### DISCUSSION

DR GEORGE W BINKLEY. Was low voltage roentgen irradiation the only therapy administered?

DR BENJAMIN LEVINE. Yes. I think that the therapeutic results have been good. One small patch has escaped the rays on one side, and some of these untreated lesions seem to be much larger.

DR JAMES R DRIVER. Sometimes solid carbon dioxide is of value in treating this disease.

#### Recurrent Urticaria Chronica Presented by DR HUGO HECHT

J C, a white man aged 34, is a teacher. After a tuberculous infection of the lungs, a thoracotomy was performed in 1937. Further treatment was taken in a sanatorium with pneumothorax. The tuberculosis is now under control. Four years after the aforementioned thoracotomy, an itching eruption appeared on the right upper quadrant of the abdomen and spread slowly over the body with alternating intensity. Cool weather is favorable for the patient. There is little itching.

When the patient was first seen, the scalp, face, back and palms were free from lesions. Many lesions are located on the neck, arms, abdomen, hips, buttocks, thighs and legs. Some lesions are visible on the soles. Each lesion is completely isolated, there is never confluence of single lesions, but often there are groups of lesions in certain regions, e g, the right upper quadrant of the abdomen. After days or weeks they disappear slowly, leaving light brown pigmentation. New lesions return at the site of the former ones. They are always the same size, 0.5 cm in diameter. The new lesion is elevated, usually oblong and yellowish red and never vesicular and never surrounded by a white zone. A few lesions are covered with a crust. These never open spontaneously, but the patient rubs them open after a bath.

The Kline exclusion reaction was negative. Urinalysis showed a 2 plus reduction of Benedict's solution. Examination of the blood for sugar showed 75 mg per hundred cubic centimeters. Tests of the urine for sugar were made from time to time, but they never showed more than a trace.

Histologic examination showed a somewhat thickened epidermis. There was some infiltration by wandering cells. The upper part of the dermis showed some edema and moderate to considerable round cell infiltra-

tion, lymphocytes and larger mononuclears predominating. In the thickened epidermis the rete cells were swollen in places, and the nuclei were larger than average. The basement membrane in many places was poorly defined. There was round cell infiltration in the upper part of the dermis, about the vessels associated with cutaneous glands and hair follicles. There was also some infiltration of the epithelium of hair follicles and of sudoriferous glands. In places numerous polymorphonuclear leukocytes were seen, although mononuclear cells predominated. Scattered throughout the infiltrate were large mononuclear cells which resembled mast cells.

External treatment with low voltage roentgen rays, ultraviolet rays from a hot quartz mercury vapor lamp and ointments resulted in no lasting improvement. Other ineffective internal treatments were an acid ash diet, then alkaline ash foods, thyroid extract and calcium and arsenical medication. A temporary improvement after twelve injections of the patient's blood could not be duplicated with a second series of injections.

#### DISCUSSION

DR GEORGE W BINKLEY. The clinical aspects that detract from a diagnosis of urticaria pigmentosa are the onset of the disease in adult life, the absence of wheezing and dermatographism and the slight amount of pigmentation. Some of the histologic features were similar to those of urticaria pigmentosa, but the changes were not pathognomonic. There was an increase in pigment in the basal layer. The dense infiltrate in the entire corium was made up of monocytes and a few giant cells. In the short time available for study, I was uncertain as to the presence of mast cells.

DR EUGENE C STERN. I think that the pigmentation could be explained by the ultraviolet rays which were given. The skin is tanned where the patient received ultraviolet radiation and is not tanned where he did not receive this treatment.

DR HUGO HECHT. If one accepts the existence of urticaria pigmentosa without mast cells, then this is a case of urticaria pigmentosa. The first biopsy specimen was taken before the patient was treated. There were big clusters of mast cells, consistent with the diagnosis of urticaria pigmentosa. In the biopsy specimen taken before the ultraviolet ray treatment there were no chromocytes, hence I think that Dr Stern's suggestion is correct. The second possibility is allergy. I showed the slide to Dr Benjamin S Kline, pathologist. He said that the disease is definitely not an allergy. I not only made patch tests, but I gave the patient elimination diets. For four months he ingested an alkaline diet and for four months an acid diet. Nothing happened. I found that twelve injections of his own blood was the best treatment, but when I tried it the second time the disease became worse. The patient had active pulmonary tuberculosis at one time. He still has a mild infection of the lungs. The cutaneous lesions come always in the same places, three or four times a year. The disease is a cutaneous reaction which flares suddenly. I think that it is an urticaria chronica caused by toxins from his tuberculosis, which irritate the sensitized skin.

#### Granuloma Annulare Presented by DR E W NETHERTON and DR W R HUBLER

W S, a white man aged 56, has had a nonpruritic papular eruption on his extremities for one year. The lesions appeared first on the wrists and then, in rapid succession, involved the dorsa of the hands, the elbows and the lower extremities.

He has been receiving injections of liver extract from his local physician for seven months without much benefit. He was taking no medicine prior to the onset of his eruption. He has had no roentgenotherapy. There is no family history of tuberculosis.

The eruption consists of flat angular brownish and yellowish red closely grouped papules, 2 mm in diameter. These cover the dorsa of the hands and the extensor surfaces of the forearms and are seen in smaller groups on the wrists, flexor surfaces of the forearms and thighs. Many of the papules are arranged in the form of small annular plaques. The skin on the dorsa of the hands appears to be slightly atrophic. Diascopic examination shows an apple-jelly-like deposit in most of the papules. Many of the lesions near the site from which the biopsy specimen was taken have disappeared.

The remainder of the physical examination reveals normal conditions.

The hemogram, blood sugar and urine were normal. The Wassermann and Kahn reactions of the blood were negative. The blood cholesterol level was 217 mg per hundred cubic centimeters. Tuberculin in a 1:5,000 dilution elicited a positive reaction. A roentgenogram of the chest revealed normal conditions.

Histologic examination of portions of the plaques from the right elbow and forearm revealed a normal epidermis, except for slight cubiform hyperkeratosis. The papillary layer was uninvolved. There was extensive focal perivascular inflammation of the corium, with decided thickening of the endothelium of the blood vessels. The focal infiltrate consisted of a reticulum of stellate cells, with a sparse infiltrate of lymphocytes. A few of the stellate cells were enlarged and had finely vacuolar eosinophilic cytoplasm.

#### DISCUSSION

DR JOHN A. GAMMEL: The eruption does not look like any granuloma annulare I have seen, and I have not seen granuloma annulare in a person of this patient's age.

DR BENJAMIN P. PERSKI: I think that on the flexor surfaces of the wrists this man shows lesions which are somewhat suggestive clinically of granuloma annulare. He has received some roentgen ray therapy, which may have altered the original appearance of the lesions, inasmuch as granuloma annulare is a relatively radiosensitive lesion. I believe that the slide shows changes which might be considered consistent with granuloma annulare. There is a granular bluish discoloration to the connective tissue in some areas—a basophilic degeneration. There are also seen some scattered epithelioid cells with a banal infiltrate interspersed among them. Histologically, the lesion could be considered granuloma annulare, although it is not clinically typical.

DR JAMES R. DRIVER: While clinically and also histologically the lesions are not typical, I favor the diagnosis as presented.

DR W. R. HUMPHREY: Dr. Fred Wise presented a 16-year-old girl with granuloma annulare before the Manhattan Dermatologic Society in 1939 (*ARCH DERMAT & SYPH* 40:291 [Aug] 1939). She had typical lesions on the hands except that the central portions of the annular plaques were covered with numerous papules. Similar small flesh-colored papules were also scattered over the body. The latter lesions were not uncommon, especially in children. The histologic picture of one of the typical lesions was that of perivascularitis. Dr.

Satenstein commented that there are many clinically typical cases of granuloma annulare in which only vascular reaction is shown histologically. In a discussion at the New York Academy of Medicine in 1929 (*ARCH DERMAT & SYPH* 19:495 [March] 1929), Dr. Howard Fox described a case from Dr. Goldenberg's service at Mount Sinai Hospital, in New York, in which the patient had a more or less generalized eruption made up of small papules, which, according to Dr. Fox, almost any dermatologist would call lichen planus. In this case, the biopsy specimen was typical of granuloma annulare. At first glance, our case might also be taken for one of lichen planus. The lesions around the site of the biopsy specimen have disappeared during the past week. As far as age is concerned, many cases of typical granuloma annulare in adults have been reported.

### METROPOLITAN DERMATOLOGICAL SOCIETY

ROYAL M. MONTGOMERY, M.D., *President*

JAMES LOWRY MILLER, M.D., *Secretary*

May 15, 1944

#### A Case for Diagnosis (Allergic Eruption?) Presented by DR. THOMAS N. GRAHAM

H. D., a white man aged 68, was first seen by me on Feb. 28, 1944. He complained of a generalized itching eruption of two months' duration. There was no history of ingestion of drugs or of allergy.

There were numerous erythematous, papular, discrete and confluent lesions, many of which presented a distinctly urticarial appearance. General physical examination showed only dental caries. The Wassermann reaction of the blood was negative. Dental roentgenograms showed abscessed teeth. The urine was essentially normal.

After removal of the infected teeth, the eruption flared up slightly and then practically disappeared, but only for about two weeks. Subsequent therapy with calcium, dilute hydrochloric acid and elimination diets failed to produce any appreciable improvement. Within the past few weeks a few of the lesions have become scaly and somewhat resemble psoriasis guttata. Above the wrists and ankles there have recently appeared a few hemorrhagic macules.

#### DISCUSSION

DR. LAIRD S. VAN DYCK: The color and distribution of the scaly papules suggest parapsoriasis, but the severe itching in a man of that age always makes one suspicious that the disease may be mycosis fungoides. A histologic report should help one to make the diagnosis.

DR. JOSEPH C. AMERSBACH: Some of the lesions on the wrist resembled lichen planus. On closer observation other lesions appeared to be infiltrated and scaling. The patient also had lesions of the scalp, and so I think that the disease may be parapsoriasis, psoriasis or lichen planus.

DR. GERALD F. MACHACEK: I have nothing to add. He has no lesion in the mouth.

DR. J. LOWRY MILLER: I believe that further observation and study of this patient will establish the diagnosis of a disease of the lymphoblastoma group. I suggest biopsy of a lymph node, studies of the blood and a roentgenogram of the chest.

DR ROYAL M MONTGOMERY From questioning it is evident that this patient does not take a normal amount of vitamin C in his diet. I suggest giving him 300 mg of ascorbic acid daily and observing the results. Vitamin C deficiency modifies the configuration of the lesions.

DR RICHARD J KELLY I favor a diagnosis first of parapsoriasis and second of lichen planus.

DR MAX WOLF (by invitation) I favor the diagnosis of parapsoriasis. The widespread distribution of small papular and macular scaly lesions over extended areas of the surface would correspond to the clinical picture of *psoriasis lichenoides chronica* or parapsoriasis.

DR THOMAS N GRAHAM I do not think lymphoblastoma a probable diagnosis in this case. The eruption so nearly disappeared at one time that only a few lesions were slightly perceptible. This occurred within a period of a few days. At times the lesions have appeared as typical wheals. A biopsy is apparently necessary to establish a diagnosis.

DR J LOWRY MILLER The spontaneous remission noted in this patient previously does not rule out lymphoblastoma. I have under observation now a patient with mycosis fungoides whose lesions come and go without treatment.

NOTE—A subsequent blood count showed 4,800,000 erythrocytes and 8,400 leukocytes per cubic millimeter. The hemoglobin amounted to 13.1 Gm per hundred cubic centimeters. The differential blood count showed 71 per cent neutrophils, 27 per cent lymphocytes and 2 per cent mononuclear leukocytes. A biopsy specimen showed chronic eczema with lichenification. There was no evidence of lymphoblastoma, lichen planus or psoriasis.

#### Alopecia Prematura Presented by DR LAIRD S VAN DYCK

A C, a 16 year old girl, the daughter of an Italian physician, has a diffuse thinning of the hair of the scalp, which began five months ago. She has had no illness for the past few years, but she was struck by an automobile two years ago, receiving an injury to the head which rendered her unconscious at the time. For two or three years previous to the onset of the rapid loss of hair, she had a thick scaly eruption on the scalp which she cured with a "dandruff cure" suggested by a neighbor. Shortly after this she noticed that her hair was falling out more rapidly each day.

The scalp shows no inflammation or scaling. There is a diffuse thinning of the hair, especially over the vertex. The remaining hair seems abnormally dry, and her nails are brittle.

#### DISCUSSION

DR JOSEPH C AMERSBACH I think that this case presents a difficult problem. There is the possibility that a girl of this age may have a regrowth of the hair which she has lost. One certainly has to consider the part emotion plays in this condition, which is undoubtedly dependent on thyroid function.

DR J LOWRY MILLER I feel that the alopecia in this patient is due to a disturbance in the functioning of the thyroid gland. The thyroid mechanism was probably adversely affected by the emotional upset. I suggest thyroid therapy unless the basal metabolic rate is definitely increased, but I do not expect that it is.

DR RICHARD J KELLY This patient should have a thorough medical examination with special attention to the thyroid.

DR THOMAS N GRAHAM I agree with what has been said in regard to this case. One must consider an infectious process, possibly a low grade staphylo-

coccic infection of the scalp. I believe that there are atrophy and scarring.

DR ROYAL M MONTGOMERY There is scarring present. For that reason the results from any type of therapy would be questionable. She was given injections of chorionic gonadotropin, a substance which used to be given for alopecia, but it is my opinion that it produced few satisfactory results.

DR LAIRD S VAN DYCK I do not have much to add, except that I share the opinion about chorionic gonadotropin as far as growth of hair is concerned. I have given it to patients for six to twelve months without beneficial results. She has abnormally dry skin, her nails are brittle, and her general appearance indicates some endocrine disturbance.

#### Tinea Ciliarum and Tinea Corporis Presented by DR ROYAL M MONTGOMERY

F C, a girl aged 9 years, has had cutaneous lesions for the past six weeks. When she came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 18, she had a circinate papule the size of a 25 cent piece with peripheral scaling and central involution on the nape of the neck. She also had a small patch on the right calf and on the right upper eyelid. On examination under ultraviolet rays with a Wood filter a number of eyelashes fluoresced on the right upper eyelid. The eyelashes and scales from the neck were cultured and yielded *Microsporon audouinii*. Her sister has tinea capitis caused by *M. audouinii*.

At present the patient's cutaneous lesions are much improved, and only slight scaling is present. The upper eyelid is also normal, with no inflammation about the hair follicles. Fluorescent hairs are present. The scalp is normal.

#### DISCUSSION

DR RICHARD J KELLY This case was very interesting. I have never seen one like it before. I agree with the diagnosis.

DR LAIRD S VAN DYCK I want to compliment the man who made the diagnosis of the lesion of the eyelid.

DR ROYAL M MONTGOMERY In the previous case which I reported (*ARCH DERMAT & SYPH* 46 40 [July] 1942), also caused by *M. audouinii*, a pustular folliculitis developed and the eyelashes were spontaneously epilated. There is still activity in the eyelashes in this case, in spite of manual epilation and the application of medication.

#### A Case for Diagnosis (Alopecia Areata, Arsenical Dermatitis?) Presented by DR J LOWRY MILLER

W W, a Negro boy aged 7 years, was admitted to the Vanderbilt Clinic on Aug 13, 1943, complaining of total loss of hair around the sides and back of the head and dermatitis involving most of the body. The dermatitis had had exacerbations and remissions over a period of two and one half years. There had been loss of hair around the sides and back of the head, with a normal sharply margined growth of hair on the top of the scalp. The dermatitis cleared with the use of a juniper tar salve, but the alopecia remained. A few scattered plugged follicles were seen, but no scarring was noted.

An examination of the blood for arsenic showed 0.22 mg of arsenic per 100 Gm of dry blood. The Wassermann reaction of the blood was negative. A biopsy specimen from the arm showed a psoriasisiform dermatitis. Mental tests showed a mental age of 2.

years an intelligence quotient of 40 and decided mental retardation

## DISCUSSION

DR LAIRD S VAN DYCK I notice in bald areas on both sides of the scalp acuminate follicular papules such as one finds in Graham Little's syndrome. I do not see how one can classify this as a case of alopecia arcata. It must be a rare form of congenital alopecia.

DR GERAUD F MACHACEK I remember that the child had a severe pyoderma.

DR THOMAS N GRAHAM I agree with Dr Van Dyck. I think that the disease is congenital.

**Sarcoid** Presented by DR J LOWRY MILLER

M L, a Negro woman aged 36, was first seen at the Vanderbilt Clinic, on April 12, 1944, complaining of lumps on the eyelids, arms and legs of two and one-half years' duration. In her past and family histories there was no mention of tuberculosis or syphilis. She was born in the city of New York. Her present trouble began with a lump forming under the skin of the left arm. A specimen for biopsy was taken from this lump. Gradually new lumps have appeared. Her general health has been good.

Examination shows about eight red oval-shaped nodules, the size of a pinhead to that of a pea, which on diascopic pressure show gray foci situated on the eyelids, upper lip and ala nasi. On the left arm and forearm are two half-dollar sized red indurated scarred (from biopsy) areas. On the lower extremities are four or five nodules as large as and even larger than a marble, movable under the skin and underlying tissues. The overlying skin is normal in appearance. The tip of the right middle finger is red, slightly tender and swollen.

General physical examination showed nothing abnormal. The blood count was normal, and the Wassermann reaction of the blood was negative. A tuberculin test (1:1,000) elicited a negative reaction. A roentgenogram of the chest showed essentially normal conditions. A biopsy showed tuberculosis cutis of the sarcoid type.

## DISCUSSION

DR GERAUD F MACHACEK The diagnosis has been substantiated by biopsy.

**Psoriasis** Presented by DR J LOWRY MILLER

W B, a Negro housewife aged 54, was admitted to the Welfare Island Dispensary on April 18, 1944, complaining of itching patches of three years' duration on the right leg and right forearm. She stated that a routine Wassermann test in 1929 elicited a positive reaction. She received three courses of ten injections each of neotarsphenamine and three courses of a bismuth preparation, after which she had a hysterectomy for fibroids. Five Wassermann tests during the past few years have all elicited negative reactions. She has received one course of injections in her arm and one in her hip in the past year. She says that she has taken no medicines by mouth. Her general health has been good.

Examination shows two palm-sized and two dime-sized red patches situated on the right shin. A quarter-sized scaly lesion is present on the right forearm. The

lesions are sharply margined with a threadlike red elevated margin running along the entire periphery of the lesion. The center of the lesion is violaceous and studded with whitish dots. There is no evidence of scarring. Mucous membranes of the mouth are clear.

Histologic examination showed an inflammatory lesion of a psoriasiform character.

## DISCUSSION

DR THOMAS N GRAHAM I think that clinically the eruption does not look like psoriasis.

DR LAIRD S VAN DYCK One feature which militates against the diagnosis of psoriasis is the depression of the central portion of the larger patch below the level of the surrounding skin. However, the scaling at the border is characteristic of psoriasis.

DR JOSEPH C AMERSBACH I suggest further observation of the case and biopsy at a future date.

DR ROYAL M MONTGOMERY I agree with the diagnosis of psoriasis. I have seen several Negroes with this disease. Dr Howard Fox reported on this subject. The scaling around the border is typical of psoriasis, but the typical micaceous scaling is not present. The pigmentation in Negroes produces a clinical appearance different from that in white patients.

DR MAX WOLF (by invitation) The patient presented in the beginning two separate large lesions covering nearly the entire anterior aspect of the right leg and two smaller lesions on the ankle. The patches had a definite bluish violaceous color and a slowly progressive raised inflammatory border with partly polycyclic outlines. Throughout the center of the lesions there were tiny "blisters," which disappeared after application of boric acid ointment, but flaky scales remained. Because of the purplish hue and the raised polycyclic border I thought of annular lichen planus. The microscopic evidences of psoriasiform changes are not corroborated by the clinical appearance of the lesions.

DR J LOWRY MILLER I suppose the diagnosis of psoriasis should be accepted because of histologic changes. Clinically the case is puzzling. I thought even of amyloidosis because of pinhead-sized foci all through the lesions.

**Pediculosis of the Eyelashes** Presented by DR J LOWRY MILLER

J H, a Negro boy aged 9 years, presented himself at the Welfare Island Dispensary, complaining of itching of the eyelids of one week's duration. Examination showed nits and pediculi in the eyelashes.

## DISCUSSION

DR RICHARD J KELLY I am interested in the case because of the child's age. Yellow mercuric oxide is indicated.

DR JOSEPH C AMERSBACH The disease is of unusual interest because of the single area affected and its location. The use of a mild antiseptic ointment, such as 0.25 per cent yellow mercuric oxide, I believe, is adequate in this case.

DR GERAUD F MACHACEK I have seen pediculosis of the eyelashes in children, evidently due to crab lice. The therapy has been described adequately.



# News and Comment

## ELIGIBILITY REQUIREMENTS FOR EXAMINATION BY THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY, INC

### I General Requirements

- 1 High ethical and professional standing
- 2 Graduation from a medical school recognized by the Council on Medical Education and Hospitals of the American Medical Association
- 3 Satisfactory completion of an internship of not less than one year in a hospital approved by the same Council or its equivalent in the opinion of the Board
- 4 A license to practice medicine
- 5 Membership in the American Medical Association or membership in a similar society recognized as having the same purpose as the American Medical Association
- 6 Citizenship in the United States or citizenship—meaning native citizens—in Canada or Cuba

### II Special Requirements

Applicants for certification by the Board are classed in two groups as follows

Group A consists of physicians who have limited their practice mainly to dermatology and syphilology for ten or more years, including a period of training satisfactory to the Board

Group B consists of physicians who have completed in approved three year period of training

In accordance with the program recommended to the various specialty boards by the Advisory Board for Medical Specialties, the following minimum requirements of special training for admission to examination have been established

A period of study, after the internship, of not less than three years. This training may be obtained as resident, fellow or graduate student in clinics, dispensaries, hospitals or laboratories recognized by the Council on Medical Education and Hospitals of the American Medical Association and approved by the American Board of Dermatology and Syphilology as competent to provide a satisfactory training in dermatology and syphilology. This period of specialized training shall include

(a) Graduate training in the basic medical sciences which are necessary for the proper understanding and treatment of the diseases involved in this specialty

Instruction in the following fundamental subjects as related to the skin is deemed advisable by the Board: embryology, histology, chemistry, physiology, bacteriology, mycology, parasitology, pathology, immunology, serology, pharmacology and materia medica and physics of physical therapy

(b) Carefully supervised clinical and laboratory experience in the specialty

(c) Annual examinations in the clinical, laboratory and public health aspects of dermatology and syphilology

Candidates who plan to take part of their training under the supervision of a specialist certified by

the Board should also be certain that he has been accepted as a preceptor of the Board. Time spent with an unqualified instructor may count only as experience and not as training

### III Credit for Work in the Armed Forces

In view of the widespread interest in specialization in dermatology by men who are or have been in service, the American Board of Dermatology and Syphilology has drawn up an outline to cover in a broad way the credits allowed toward training and experience of candidates for their military work. In view of the variability of dermatologic work and the differing conditions under which it was carried on by commissioned medical officers of the Army, Navy and Public Health Service, the Board is unable to issue specifications for eligibility for examination to cover every situation that has arisen in the experience of every candidate, but the following general statements can be made

1 Full credit will be given for dermatologic training in approved institutions, which preceded the military service

2 Full time dermatologic military service may be credited, at the discretion of the Board, for part, or in some cases all, of two years of the three required years of training. But at least one year of the three years' required training, to include instruction in the fundamental subjects deemed essential for an adequate dermatologic education, must be spent in one of the institutions approved for a three year training program by the Board and by the Council on Medical Education and Hospitals of the American Medical Association

3 In any event, the Board strongly urges that the candidate supplement his military experiences by a further period of systematic and supervised dermatologic training before the examination

4 A credit for one year as experience has also been voted by the Board for one year of any military service. Thus a medical officer who passes the examination at the end of three years of training will receive his certificate one year later instead of at the completion of a total of five years' training and experience. Dermatologic work while in the armed forces, not credited as training, may satisfy part or all of the remaining year of required dermatologic experience

5 For commissioned officers the total fee will be \$50 instead of \$75, of this, \$25 must accompany the application. The examination fee of \$25 is payable when the candidate is notified that his application has been approved by the Board. These fees are not returnable

In order that a prospective candidate may ascertain the credit he will receive for his military service, it will be necessary for him to fill out a special form which may be obtained from the Secretary

### Dearth of Opportunities for Training

The present greatly increased demand for training by recently discharged veterans has created a dearth of opportunities in accredited institutions



It is possible that there are other institutions which can qualify to train suitable applicants at least partially. It is also undeniable that many capable teachers have not as yet applied to be preceptors so that they will also be available to supervise part of the training of promising candidates.

For further information apply to the secretary, Dr George M. Lewis, 66 East Sixty-Sixth Street, New York 21.

### GENERAL NEWS

**Section on Dermatology and Syphilology, American Medical Association**—Applications for places on the program of the Section on Dermatology

and Syphilology at the next Annual Session of the American Medical Association are now being received. All Fellows of the American Medical Association are eligible. The program will be assembled in the early part of January 1946. Essayists who are not Fellows of the American Medical Association may be accepted by invitation.

All applications which were received for the 1945 meeting, which was not held because of the war, will be considered by the committee.

Applications should be addressed to Dr Nelson Paul Anderson, Secretary of the Section on Dermatology and Syphilology, 2007 Wilshire Boulevard, Los Angeles 5, Calif.

## Book Reviews

**Approved Laboratory Technique** By John A. Kolmer, M.D., LL.D., and Fred Boerner, V.M.D. Fourth edition. Price, \$10. Pp 1,017, with 548 black and white illustrations. New York: D. Appleton-Century Company, Inc., 1945.

No matter how well trained and how well read a physician may be, there are times when he must find himself in a void when he studies laboratory reports, which are becoming more and more frequent and complicated as medical science advances. While dependence on laboratory procedure is particularly true of the physician of the hospitalized patient, it also is becoming increasingly necessary to the physician in resolving many of the problems in diagnosis which are so intriguing in the private office. Also, many physicians are unaware as to what is involved in the laboratory when they make requests for laboratory examinations. Every dermatologist should know at least what was behind the scenes in the laboratory, teaching, particularly, should be prepared to round out their presentations to students in this connection. In these circumstances, the busier the physician, the more welcome is a book—such as this one by Kolmer and Boerner—which will fill the void.

The authors grant that the book does not cover the changes due to disease and their interpretation, it is confined largely to methods and normal values. This will be disappointing to most dermatologists, particularly the absence of "interpretation." However, the

dermatologist scattered through the book, though, are subjects of which he should have knowledge. Of high importance is the separate section which deals with methods for the collection and handling of material for bacteriologic examinations. The many tests of serum and spinal fluid for syphilis are exhaustively and authoritatively presented by such experts as Kolmer and Boerner. By way of illustrating special needs of dermatologists, the following subjects deserve mention: technic of sternal biopsy, tests for porphyrin and melanin in the urine, the Fishberg test for hepatic function (which is so important in the rapid treatment of syphilis), the congo red test, the fluorescent dye method for demonstrating *Mycobacterium tuberculosis* and *Mycobacterium leprae*, the detection of amebas, the oil method for demonstrating the presence of mites, tests for heterophile antibodies and technics for determining the blood cholesterol level of blood, the sulfanilamide content of urine, the concentration of vitamins in blood and urine and the bromide content in the blood and urine. The hematologic methods that are described concern the dermatologist in the difficult field of the leukoses and to a less degree in the erythrocytoses (sickle cell anemia, hypochromic anemia and others). For the purposes of the dermatologist the section on mycology is decidedly inferior to that which is offered in the texts sponsored by dermatologists. No doubt, the inaccuracies and organization of this new section will be corrected in future editions. The section on animal

# Directory of Dermatologic Societies \*

## INTERNATIONAL

### TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

Oliver S Ormsby, President, 25 E Washington St, Chicago  
Paul A O'Leary, Secretary-General, 102-2d Ave S W, Rochester, Minn  
Place New York Time Postponed indefinitely

### PAN AMERICAN MEDICAL ASSOCIATION, SECTION OF DERMATOLOGY AND SYPHILOLOGY

J J Eller, President, 745-5th Ave, New York  
Austin W Cheever, Secretary, 464 Beacon St, Boston

## FOREIGN

### BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY (CANADIAN BRANCH)

D E \*H Cleveland, President, 925 W Georgia St, Vancouver, B C  
Donald H Williams, Secretary-Treasurer, 925 W Georgia St, Vancouver, B C

### HAWAII DERMATOLOGICAL SOCIETY

James T Wayson, President, Territorial Office Bldg, Honolulu  
Harry L Arnold Jr, Secretary, 881 Young St, Honolulu

### ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

M Sydney Thomson, President, King's College Hospital, Denmark Hill, London S E 5, England  
Geoffrey R Edwards, Secretary, 1 Wimpole St, London W 1, England

### SOCIEDAD MEXICANA DE DERMATOLOGIA

Mario Salazar Mallen, President, Ignacio Ramirez 11, Mexico, D F, Mexico  
Fernando Latapi, Permanent Secretary, Zacatecas 220-6, Mexico, D F, Mexico

## NATIONAL

### AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Clyde L Cumber, Chairman, 1422 Euclid Ave, Cleveland  
Nelson P Anderson, Secretary, 2007 Wilshire Blvd, Los Angeles

### AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

George M MacKee, President, 999-5th Ave, New York  
Earl D Osborne, Secretary, 471 Delaware Ave, Buffalo, N Y

### AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E 54th St, New York  
George M Lewis, Secretary-Treasurer, 66 E 66th St, New York

### AMERICAN DERMATOLOGICAL ASSOCIATION

Fred D Weidman, President, Medical Laboratories, University of Pennsylvania, Philadelphia  
Harry R Foerster, Secretary, 208 E Wisconsin Ave, Milwaukee

### SOCIETY FOR INVESTIGATIVE DERMATOLOGY

Henry E Michelson, President, 715 Medical Arts Bldg, Minneapolis  
S William Becker, Secretary, 55 E Washington St, Chicago 2

## SECTIONAL

### CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Frank R Menagh, President, Henry Ford Hospital, Detroit  
C E Reyner, Secretary-Treasurer, Henry Ford Hospital, Detroit  
Place Harper Hospital, Detroit. Time April 27, 1946

### MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

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- Anodontia See Teeth, development
- Anthrax, human, treatment with penicillin, 272
- Antigens and Antibodies See also Lipoids, and under specific antigens and reactions  
role of lymphocyte in antibody formation, 408
- Anus adenoma of apocrine sweat glands (hidradenoma) of anal canal, 120
- Apparatus See Instruments
- Armed Forces Personnel See also Military Medicine, Naval Medicine, etc  
Army Air Forces dermatology program, \*6
- Armies See Aviation and Aviators, Military Medicine
- Arms See also Extremities, etc  
paraffinoma, 42
- Arnold, H L, Jr Differentiation of lepromatous from "neural" leprosy, basis, method and report of 5 cases \*354  
James Thomas Wayson, 183  
Lupus vulgaris, 67  
Psoriasis, vesicular lichen planus or herpes, 67  
Purpura annularis telangiectodes (Majocchi), case for diagnosis, 66  
Syphilitic juxta-articular nodules combined with leukoderma of wrists palms and feet, 66  
Virus papillomas in burn scars, case for diagnosis 66
- Arsenic and Arsenic Compounds See also Arsphenamines, Tryparsamide  
acute yellow atrophy of liver in early syphilis case report with summary of literature 120  
alopecia areata or arsenical dermatitis, 126  
arsenical keratoses of palms and soles or trophic ulcer of foot, 126  
colloidoclastic shock following injection of oxophenarsine hydrochloride (mapharsen), report of case \*395  
leukomelanoderma following arsenical dermatitis (malignant melanoma) 64  
multiple benign superficial epithelioma 281  
prevention of post-arsphenamine jaundice, 412  
Therapy See under Lupus erythematosus, Syphilis
- Arsphenamines dermatitis medicamentosa, case for diagnosis, 139  
Therapy See under Syphilis
- Arteries See Aneurysm, Periarthritis, Vasomotor System, etc
- Arthritis, polyarticular and osteomyelitis due to granuloma inguinale, 35
- Ascorbic Acid, colloid degeneration of skin (colloid milium), report of case with observations on ascorbic acid therapy \*180
- Aspergillus, onychomycosis and dermatomycosis caused by *Trichophyton rubrum* and *Aspergillus nidulans* \*162
- Asthenia, tropical anhidrotic, 37
- Astrachan, G D Sarcoid, late secondary syphilis 216
- Athlete's Foot See Ringworm
- Atopy See Anaphylaxis and Allergy
- Atrophoderma See Atrophy
- Atrophy See also Acrodermatitis chronica atrophicans and under names of organs and regions, as Liver, etc  
cutaneous, case for diagnosis, 145  
macular of buttocks, 284  
recurrent syphilis, macular atrophy secondary to syphilis, 212  
with disseminated granuloma annulare, 278
- Aviation and Aviators, Army Air Forces dermatology program, \*6
- Avitaminoses See under Vitamins
- Axilla See Sweat Glands
- Ayres, S, Jr Adenoma sebaceum, 282  
Cutaneous atrophy, case for diagnosis, 145  
Generalized monilliasis and trichophytosis 277  
Mycosis fungoides or leukemia cutis, 54  
Pseudoatrophoderma coli et corporis, 280  
Rosacea case for diagnosis 144  
Sarcoid, 142
- Ayres, S III Congenital ectodermal defect 418  
Periarthritis nodosa, case for diagnosis 422
- BCG See under Tuberculosis
- Bacillus See Bacteria
- Back, papulonecrotic tubercloid including involvement of face, chest and back, 205
- Bacteria See also Meningococci, Staphylococci, Tubercle Bacilli, etc  
Anthrax See Anthrax  
Calmette Guérin See Tuberculosis  
destruction of nicotinic acid, 409  
Diphtheria See Diphtheria  
Ducrey's See Chancroid  
Erysipelothrix See Erysipeloid  
Leprosy See Leprosy  
Tularensis See Tularemia
- Bactericides See Germicides
- Bacterid, pustular, case for diagnosis, 296
- Bagby J W Tropical lichen planus-like disease, \*1
- Baldness See Alopecia
- Barbital and Barbital Derivatives dermatomyositis, psychoneurosis, dermatitis medicamentosa (pentobarbital sodium), cutis marmorata, 215
- Barksdale, F F Erythema perstans, 39  
Scleroderma, 44
- Baths steam, treatment of ichthyosis, \*178  
whirlpool, trench foot, 186
- Bazin's Disease See Erythema induratum
- Beard See Hair
- Becker S W Lichen syphiliticus (extragenital infection) or lichen scrofulosorum, 195
- Beldelmin F Steatocystoma multiplex, 296
- Benadryl See Urticaria
- Benzpyrene, effect of 34 benzpyrene on regenerating epidermis of mice, 35
- Benzyl Benzoate See Scabies
- Berberian, D A Cutaneous leishmaniasis (oriental sore), treatment with quinacrine hydrochloride, \*26
- Bereston, F S Onychomycosis and dermatomycosis caused by *Trichophyton rubrum* and *Aspergillus nidulans* \*162
- Berger, J P Effect of feeding lipotropic substance to patients with xanthelasma, \*252
- Besnier-Boeck's Disease See Sarcoidosis
- Biberstein, H H Immunization therapy of warts, 34
- Binkley G W Postsyphilitic dyschromia, late dyschromic pinta (treated), 415
- Birthmark See Nevus
- Bismuth and Bismuth Compounds fixed bismuth dermatitis, case for diagnosis, 275  
systemic manifestations of bismuth toxicity 405  
Therapy See under names of various diseases, as Lupus erythematosus, Syphilis, etc
- Blaisdell J H Pityriasis lichenoides et varioliformis acuta, 136
- Blanket Electric See Thermotherapy
- Blastomycosis, 62 See also Coccidioidomycosis, Monilliasis  
colloidoclastic shock following injection of oxophenarsine hydrochloride (mapharsen), report of case, \*395  
or sporotrichosis, 142  
systemic 198
- Blennorrhagia See Keratosis blennorrhagica
- Blepharitis See Oculitis
- Blood Diseases See Leukemia, etc  
fats and lipoids effect of feeding lipotropic substance to patients with xanthelasma, \*252  
proteins, effect of tuberculous and sensitized sera and serum fractions on development of tubercles in chorioallantoic membrane of chick 408  
sugar carbohydrate metabolism and skin, \*301  
vessels periphlebitis perivascularitis nodularis necroticans or erythema induratum of unusual type 133  
vessels, vasculitis or periarthritis nodosa 134
- Bluefarb, S M Dermatofibrosarcoma protuberans with dementia paralytica tabetic type, 202
- Boardman W P Parapsoriasis lichenoides (Brocq), case for diagnosis, 140
- Boeck Sarcoid See Sarcoidosis
- Boll, Jericho See Leishmaniasis

- Bones See under names of bones  
Diseases See Osteomyelitis, etc  
Marble See Osteosclerosis fragilis
- Boor Reviews  
Approved Laboratory Technique, J A Kolmer and I Boerner, 429  
Doctors at War, edited by M Fishbein, 71  
Hair and Scalp Clinical Study (with Chapter on Hirsuties), A Savill, 220  
Male Hormone, P de Kruif, 71  
Medical Uses of Soap Symposium, G T Halberstadt and others, edited by M Fishbein, 219  
Modern Cosmeticology, R G Harry, 219  
Modern Syphilotherapy with Particular Reference to Salvarsan A Neisser, translated by I von Sazenhofen Wartenberg, 300  
Outline of Amino Acids and Proteins, edited by M Sahyun, 300  
Penicillin Therapy Including Thyrothricin and Other Antibiotic Therapy, J A Kolmer, 220
- Books See Literature
- Bordet-Wassermann Reaction See Syphilis
- Bowen's Disease See Cancer, precancer
- Brain, cerebrovascular accidents following epinephrine injections, 272  
Syphilis See Neurosyphilis
- Bright's Disease See Nephritis
- Bromide and Bromine, bromoderma, 191
- Bromoderma See Bromide and Bromine
- Bubo, Chancroid See Chancroid  
Climatic See Lymphogranuloma Venereum
- Bubonulus See Granuloma inguinale
- Bullosis See Vesication
- Burns, value of sulfonated oils in treatment of burns and other denuded surfaces, 411  
virus papillomas in burn scars, case for diagnosis, 66
- Burpau, C Paraffinoma, 42  
Superficial benign basal cell epithelioma, 46
- Buschke's Disease See Scleroderma
- Butcher, E O Pigmentation of hair on transplanted skin in hooded rats, \*347
- Butterworth, T Achromic nevus or atypical hydroa puerorum, 297  
Fungous infection of back of neck, 293  
Necrobiosis lipoidica without diabetes, 295  
Pustular bacterid, case for diagnosis, 296  
Schamberg's progressive pigmentary dermatosis, 295  
Stenocystoma multiplex, 296
- Buttocks herpes simplex of, 54  
macular atrophy of, 284
- Cadmium Chloride See Ringworm
- Calcification, calcinosis cutis or osteopikilosis, 128  
calcinosis universalis in infant, 122  
generalized calcinosis cutis without involvement of muscles or nerves, 189
- Calcinosis See Calcification
- Calcium and Calcium Compounds, Penicillin See Penicillin
- Callosities See Keratosis
- Calmette Guérin Tuberculin See Tuberculosis
- Camphor, Therapy See Ringworm
- Cancer See also Epithelioma, Sarcoma, and under names of organs and regions, as Esophagus, etc.  
Irritation and carcinogenesis, 121  
precancer, Bowen's disease, 289  
precancer, Bowen's disease of penis, late latent syphilis (treated), 413  
pseudocarcinomatous hyperplasia in primary secondary and tertiary cutaneous syphilis, 186
- Candida See Monilliasis
- Cantares O Is penicillin a photosensitizing agent? \*17
- Cannon A B Arsenical keratoses of palms and soles or trophic ulcer of foot, 126
- Carate See Pinta
- Carbuncle See Anthrax
- Carcinoma See Cancer
- Cardiovascular System See Blood vessels, Heart, Vasomotor System, etc
- Caro, M R Cutaneous neuroma, 202  
Lichen striatus, 199
- Carpenter, C C Treatment of pityriasis rosea with Trichophyton extract, 184
- Carrick, L Use of Benadryl for urticaria and related dermatoses, preliminary report, \*243
- Catechol See Pyrocatechol
- Cells See Tissue
- Cerebrospinal Fluid See Spinal Puncture
- Cerebrum See Brain
- Cervix See under Uterus
- Cevitamic Acid See Ascorbic Acid
- Chambers, G Clinical investigation of new cutaneous entity, \*226
- Chancre, Lymphogranulomatous See Lymphogranuloma Venereum  
Soft See Chancroid
- Chancroid, experimental prophylaxis and treatment of chancroidal infection, 121  
infectivity of Hemophilus ducreyi for rabbit and development of skin hypersensitivity, 405  
of cervix, 410
- Cheever, A W Lichen nitidus, 141  
Nevus linearis, case for diagnosis, 141
- Chemotherapy See under names of diseases and chemotherapeutic agents, as Coccidioidomycosis, Fusospirochetosis, Impetigo, Neurosyphilis, Penicillin, Skin, diseases, Sulfonamides, Syphilis, etc
- Chest See Thorax
- Chickenpox, herpes zoster and acute anterior polymyelitis, 410
- Children See also Infants  
erythema nodosum in, 186  
herpetic stomatitis in infants and children, 37  
lichen sclerosus et atrophicus in childhood, \*351
- Chlorine and Hypochlorite Derivatives, urticaria caused by chlorinated drinking water, 272
- Chorioallantoic Membrane See Tubercle Bacilli
- Chromoblastomycosis See Blastomycosis
- Chromomycosis See Blastomycosis, Mycosis
- Cicatrix, virus papillomas in burn scars, case for diagnosis, 66
- Cilia See Eyelashes
- Cipollaro, A C Mycosis fungoides, 58  
Tinea capitis, 56
- Clare, H C Dermatitis from dehydration of potatoes, \*9
- Climacteric See Menopause
- Clothing, cotton hose as vehicle for fungicide in treatment of athlete's foot, 36
- Coccidioidomycosis, 37
- Cohen, D Congenital ectodermal defect or monilliasis, 194  
Dermatitis herpetiformis treated with acetarsone, 292  
Psoriasis simulating stasis dermatitis, 65  
Seborrheic dermatitis, case for diagnosis, 64  
Tuberculosis miliaris disseminata faciei, 59
- Cole, H N Adenoma sebaceum (Pringle type forme fruste), 422  
Dystrophila mediana canaliformis, 418  
Lupus erythematosus hypertrophicus, 417  
Lupus vulgaris erythematosus of Leloir, case for diagnosis, 417  
Pyoderma gangrenosum associated with nonspecific ulcerative colitis, 416  
Scleroderma en coup de sabre, 420
- Colimodio, S Bowen's disease of penis, late latent syphilis (treated), 413  
Sarcoidosis, 413  
Sarcoidosis, tuberculoid leprosy, late latent syphilis (treated), 413
- Colitis, pyoderma gangrenosum associated with nonspecific ulcerative colitis, 416
- Colloid Millium See under Skin
- Colloidoclastic Shock See Anaphylaxis and Allergy



- Colon Inflammation See Colitis
- Combes I C Angioma serpiginosum, case for diagnosis, 206
- Communicable Diseases See Syphilis, etc
- Complement Fixation See under Lymphogranuloma Venereum, Syphilis
- Congress See Societies
- Conjunctiva nevus flammeus associated with conjunctival telangiectasia and possible early choroidal tumor, 35
- Conjunctivitis, dermatitis venenata following use of penicillin ointment \*341
- Cooking and Eating Utensils occupational dermatitis caused by germicidal powder Microline (used in dishwashing), 107
- Coombs R B Penicillin ointment studies on stability relative to potency and on sensitivity of human skin to patch tests with ointment \*216
- Copper penetration of surface tissues with copper by iontophoresis, penetration with organic and inorganic copper salts and use of detergents in iontophoresis \*96
- Cornblet T Blastomycosis 12
- Congenital ectodermal defect or moniliasis, 191
- Dermatitis herpetiformis treated with acetarsone 292
- Hyperpigmentation of abdomen (von Gierkes disease hyperinsulinism) 61
- Multiple superficial epitheliomatosis, 249
- Lymphogus or dermatitis herpetiformis, 200
- Platyias lichenoides et varioliformis acuta case for diagnosis 288
- Psoriasis simulating stasis dermatitis 65
- Seborrheic dermatitis, case for diagnosis 61
- Cornea relation of eye to immunity in experimental syphilis, development of immunity after primary intracorneal inoculation influence of non-specific inflammatory reaction in cornea on development of immunity in that tissue after intratesticular inoculation, 121
- Correction in transcript of article by Dr Francesco Ronchese entitled A Case for Diagnosis (Acquired Localized Trichorrhexis [Trichoclasia], Keratosis Pilaris?) (Arch Dermat & Syph 51 112 [June] 1915) 11
- Corson E F Dermatitis herpetiformis, case for diagnosis 190
- Keratosis palmaris et plantaris 190
- Corynebacterium Diphtheriae See Diphtheria
- Cosmetics hair lacquer dermatitis in infants from contact with mother's hair 272
- urticaria from perfume \*11
- Costello, M J Acrodermatitis perstans of Hallopeau treated successfully with thyrothricin, 57
- Congenital cyst of frontal bone, 56
- Erysipeloid treated successfully with injections of penicillin, report of case, \*400
- Ichthyosis or lichen planus hypertrophicus, 135
- Nevus pigmentosus et pilosus, 214
- Papulonecrotic tubercullid including involvement of face chest and back 205
- Periphrlebitis, perivascularitis nodularis necroticans or erythema induratum of unusual type 133
- Purpura annularis telangiectodes (Majocchi's disease?) treated successfully with gold sodium thiosulfate, 216
- Pyoderma faciale following dermatitis venenata, 215
- Tuberculosis verrucosa cutis in patient with advanced pulmonary tuberculosis, 136
- Verruca plana or lichen planus, 192
- Counter, C E Granuloma annulare with disseminate lesions 278
- Lupus erythematosus, discoid type, 50
- Couperus, M Lichen sclerosus et atrophicus, 142
- Creeping Eruption results of treatment with fuadin, \*174
- Cummer C L Sarcoidosis, 414
- Curth H O Abraham Buschke 32
- Curth, W Abraham Buschke, 32
- Curtis A C Beta dimethylaminoethyl benzhydryl ether hydrochloride (Benadryl) in treatment of urticaria \*239
- Effect of feeding lipotropic substance to patients with antheleasms, \*252
- Curtis, G H Contact dermatitis of eyelids caused by antioxidant in rubber fillers of eyelash curlers, report of 7 cases, \*262
- Cushing Syndrome, 63
- Cutis Marmorata See Skin
- Cysts See under names of organs and regions, as Frontal Bone, Hand, Synovial Membrane, etc
- Dandruff See Seborrhea
- Darier's Disease See Keratosis follicularis
- Darier Roussy Sarcoid See Sarcoidosis
- Dark Adaptation See Eyes, accommodation and refraction
- Darling's Disease See Histoplasmosis
- D'Avanzo, C S Impetigo bullosa in tropics, \*28
- Dicker H B Generalized calcinosis cutis without involvement of muscles or nerves 189
- Deficiency Diseases See Nutrition, Pellagra, Vitamins etc
- Degeneration Amyloid See Amyloidosis
- Colloid See under Skin
- Dehydration in histologic embedding eliminated by use of water-soluble synthetic plastic, 120
- of Food See Food, dried
- Dementia Paralytica, dermatofibrosarcoma protuberans with dementia paralytica tabetic type 262
- Dentition See Teeth
- Depigmentation See Pigmentation
- Dermacentor Variabilis See under Tularemia
- Dermatitis See also Acrodermatitis, Eczema, Neurodermatitis, etc
- Acneform See Acne
- Actinica See under Light
- Arsphenamine See Arsphenamines
- Atopic See Eczema, Neurodermatitis
- Atrophicus See Atrophy
- Blastomycetic See Blastomycosis
- chronic recurrent papulopustular dermatitis related to vitamin deficiency 127
- Contract See Dermatitis venenata
- dykeratoid dermatosis case for diagnosis, 46
- Eczematous See Eczema
- exfoliativa in South Pacific \*75
- faciella or neurodermatitis circumscripta 138
- faciella or neurotic excoriations, 65, 137
- factors influencing dermatitis in coal miners 187
- Gangraenosa See Gangrene
- herpetiformis case for diagnosis 190
- herpetiformis or pemphigus, 200
- herpetiformis, polycythemia with unusual eruption, \*172
- herpetiformis treated with acetarsone 292
- lichen planus, lichenoid purpuric dermatitis (Gougerot and Blum), avitaminosis A or parapsoriasis, 139
- localized sensitivity to crude penicillin, \*382
- match dermatitis on chest and secondary and grease allergy of face, 68
- Medicamentosa See also under names of drugs as Arsenic and Arsenic Compounds Arsphenamines, Barbitol and Barbitol Derivatives Bismuth and Bismuth Compounds, Bromide and Bromine, Phenolphthalein and Phenolphthalein Derivatives, Penicillin, Trypsinamide, etc
- medicamentosa associated with secondary polycythemia, report of case, \*389
- medicamentosa, case for diagnosis 139
- medicamentosa (pentobarbital sodium), dermatomyositis, psychoneurosis cutis marmorata, 215
- Multiformis See Dermatitis herpetiformis
- Occupational See under Industrial Diseases
- psoriasis simulating stasis dermatitis, 65
- Rhus See Rhus poisoning
- Roentgen Ray See under Roentgen Rays
- Seborrheic See Seborrhea
- Solar See under Light
- Venenata See also Resins, etc
- venenata, hair lacquer dermatitis in infants from contact with mother's hair 272
- venenata, contact dermatitis due to pigment in zinc chromate primer 279
- venenata, contact dermatitis due to "Protek" 279
- venenata, contact dermatitis due to resinous ingredients of zinc chromate primer and certain lacquers, 279

- Dermatitis—Continued**  
 venenata, contact dermatitis of eyelids caused by antioxidant in rubber fillers of eyelash curlers, report of 7 cases, \*262  
 venenata, "diaper rash" due to Perm-Aseptic, 408  
 venenata following use of penicillin ointment, \*384  
 venenata, occupational dermatitis caused by germicidal powder "Microlene," 407  
 venenata, overtreatment dermatitis, 408  
 venenata, psoriasis, contact dermatitis, 47  
 venenata, pyoderma faciale following, 215  
**Dermatofibrosarcoma protuberans** with dementi paralytica tabetic type, 202  
**Dermatologic societies** directory of, 72, 430  
**Dermatology, American Board of Dermatology and Syphilology**, 70, 269  
 Army Air Forces dermatology program, \*6  
 dermatologic practice in station hospital in Southern California, comparison with private practice, \*21  
 dermatologic therapy in tropics, 273  
 eligibility requirements for examination by American Board of Dermatology and Syphilology, Inc., 428  
 history, erythema nodosum in eighteenth century, case of child Mozart 33  
 in army station hospital serving in Italy, \*335  
 one hundredth anniversary of first American textbook of, 117  
 tropical course in, 70, 268  
**Dermatomycosis** See Mycosis, cutaneous, Ringworm  
**Dermatomyositis**, psychocurosis, dermatitis medicamentosa (pentobarbital sodium), cutis marmorata, 215  
**Dermatophytes** See Fungi  
**Dermatophytosis** See Mycosis, cutaneous  
**Dermatoses** See Dermatitis, Eczema, Skin, diseases, etc  
**Derris**, allergy from timbo (*Lonchocarpus* H. B. K.) (case with reaction to Derris, also), 409  
**Detergents** See also Ammonia and Ammonia Compounds, Soaps  
 penetration of surface tissues with copper by iontophoresis, penetration with organic and inorganic copper salts and use of detergents in iontophoresis, \*96  
 value of sulfonated oils in treatment of burns and other denuded surfaces, 411  
**Diabetes Mellitus**, necrobiosis lipoidica diabetorum, 11 291  
 superficial gangrene in adolescent diabetes, 187  
**Diapers** See Dermatitis venenata  
**Diet and Dietetics** See Nutrition, Vitamins, and under names of food  
**Diethylstilbestrol** See Estrogens  
**Dihydroxyhexachlorodiphenylmethane** See Phenylmethane  
**Diphtheria**, cutaneous medical experiences in North Africa, 1913-4, 187  
**Directory of dermatologic societies**, 72 430  
**Dishwashing** See Cooking and Fating Utensils  
**Disk, Optic** See Nerves optic  
**Dixon H. A.** Intensive treatment of early syphilis with oxophenarsine hydrochloride by multiple injections, \*155  
**Dobes, W. L.** Penicillin in treatment of cutaneous disease, \*14  
**Dolce F. A.** Creeping eruption, results of treatment with fuanlin, \*171  
**Dorne, M.** Lupus erythematosus case for diagnosis 196  
 Parapsoriasis 288  
 Pemphigus case for diagnosis, 60  
**Driver J. R.** Adenoma sebaceum (Pringle type forme fruste) 122  
 Dystrophia mediana cranialis 418  
 Lupus erythematosus hypertrophicus 417  
 Lupus vulgaris erythematosus of Leloir case for diagnosis 417  
 Pyoderma gangrenosum associated with nonspecific ulcerative colitis 416  
 Scleroderma en coup de sabre 420  
**Drugs, Eruptions** See under names of drugs, as Arsenic and Arsenic Compounds, Arsphenamines, Barbitol and Barbitol Derivatives, Bismuth and Bismuth Compounds, Bromide and Bromine, Penicillin, Phenolphthalein and Phenolphthalein Derivatives, Sulfonamides, Tryparsamide, etc  
**Ducrey Vaccine** See under Chancroid  
**Duemling, W. W.** Cutaneous diseases in South Pacific, observations among military forces, \*75  
**Duhring's Disease** See Dermatitis herpetiformis  
**Durand-Nicolas-Favre's Disease** See Lymphogranuloma Venereum  
**Dyschromia** See Vitiligo  
**Dysentery, Amebic** See Amebiasis  
**Dyshidrosis** See under Sweat Glands  
**Dyskeratosis** See Skin, abnormalities  
**Dystrophy** See Nails  
**Ear, rosacea and rhinophyma** (nose and ear lobes), 201  
 treatment of external otitis, local sulfonamide therapy, 272  
**Ebert, M. H.** Lepra maculoanesthetica, 290  
 Mycosis fungoides in Negro, 63  
 von Recklinghausen's disease, 62  
 Tuberculid, case for diagnosis, 197  
**Ectodermal Defect**, congenital, 418  
 congenital, or monilliasis, 194  
 ectodermal dysplasia with partial anodontia, 272  
 epidermodysplasia hystricoidis bullosa, report of case with histopathologic study, \*328  
 hereditary ectodermal dysplasia, 272  
**Eczema, Atopic** See Neurodermatitis  
 death caused by vaccinia in eczematoid infant, 186  
 demonstration of effect of nutrition on skin, 401  
 generalized vaccinia in eczematous child, demonstration of virus and comment on Kaposi's varicelliform eruption" 405  
 Seborrheic See Seborrhea  
 use of Benadryl for urticaria and related dermatoses, preliminary report, \*243  
**Edema** See also under names of organs and regions  
 hereditary, congenital hereditary lymphedema (Milroy's disease), 187  
**Eichenlaub, F. J.** Granuloma inguinale, 49  
 Lichen planus atrophicus, 41  
 Mycosis fungoides, 49, correction, 185  
 Parapsoriasis 43  
 Peculiar alopecia symptomtica, 41  
 Syringocystadenoma, 45  
**Elastic tissue** semblance to mycelium in potassium hydroxide preparations, \*115, 401  
**Electric Blanket** See Thermotherapy  
**Welder** See Industrial Diseases  
**Electrocoagulation** See under names of various diseases  
**Electrosurgery** See under specific headings  
**Emmons, C. W.** Relation of ultraviolet-induced mutations to speciation in dermatophytes \*257  
**Endocrine Therapy** See under names of glands and hormones, as Adrenal Preparations, Insulin, etc  
**Epidermis** See Skin  
**Epidermodysplasia hystricoidis bullosa**, report of case with histopathologic study, \*328  
**Epidermolysis bullosa**, case for diagnosis, 285  
 bullosa hereditaria, 282  
 bullosa, suggestion as to possible causation \*317  
**Epidermophyton** See Mycosis, cutaneous  
**Epinephrine** See Adrenal Preparations  
**Epithelioma of lip**, case for diagnosis 144  
 multiple benign superficial epithelioma 281  
 multiple superficial epitheliomatosis, 289  
 probably arising from sweat glands 43  
 squamous cell epithelioma, case for diagnosis, 44  
 superficial benign basal cell epithelioma 46  
 xeroderma pigmentosum with precocious malignancy 121

- Epstein, E. Dermatologic practice in station hospital in Southern California, comparison with private practice, \*21
- Erdoes-Brown, M. Hodgkin's disease with pruritus, 194
- Premycosis fungoides, 287
- Eruptions. See under Arsenic and Arsenic Compounds, Arsphenamines, Skin, diseases, etc.
- Erysipeloid treated by penicillin, 2 cases, 412  
treated successfully with injections of penicillin, report of case, \*100
- Erysipelothrix. See Erysipeloid
- Erythema, 209  
induratum of unusual type, periphlebitis or perivasculitis nodularis necroticans 133  
multiforme, case for diagnosis, 143  
multiforme, recurrent confined to 1 finger, 57  
multiforme, report of case of severe erythema multiforme with involvement of mucous membranes treated with penicillin \*91  
multiforme, use of methenamine in dermatology, 185  
nodosum, 287  
nodosum, etiology of, 188  
nodosum in children, 186  
nodosum in eighteenth century, case of child Mozart, 33  
perstans, 39
- Erythrasma. See Microsporiasis
- Erythrocytes. See Polycythemia, etc
- Erythroderma Exfoliatum. See Dermatitis exfoliativa
- Ichthyosiform. See Ichthyosis
- Maculopapular. See Parapsoriasis
- Esophagus carcinoma in British West Indian and Panamanian Negroes, study of incidence etiological factors and pathologic anatomy in 50 cases 406  
generalized progressive scleroderma with involvement of glottis and esophagus, 196
- Ethylomene. See Lymphogranuloma Venereum
- Estrogens, effect of endocrine substances on adult human scalp, \*323  
treatment of post-irradiation necrosis, 110
- Estrone. See Estrogens
- Eveland F. B. Lupus erythematosus, case for diagnosis, 294
- Extremities. See also Arms, Legs, etc  
blood supply, epidermolysis bullosa, suggestion as to possible causation \*317  
blood supply, use of fluorescein method in establishment of diagnosis and prognosis of peripheral vascular diseases, 120  
cutaneous and subcutaneous lesions of lower limbs in connection with veins differential diagnosis \*376  
folliculitis of pyoderma, perifolliculitis capitis abscedens et suffodiens, 212
- Ulcers. See Ulcers
- Eyebrows, ringworm of, \*116
- Eyelashes, contact dermatitis of eyelids caused by antioxidant in rubber fillers of eyelash curlers, report of 7 cases, \*262  
pediculosis of, 427  
tinea ciliarum and tinea corporis 426
- Eyelids, chronic blepharitis (cause, therapy?), 192  
contact dermatitis caused by antioxidant in rubber fillers of eyelash curlers, report of 7 cases, \*262  
dermatitis venenata following use of penicillin ointment, \*384
- Eyes. See also under names of special structures and diseases of eye  
accommodation and refraction disturbances of visual adaptation and their clinical significance 36
- Face, dermatitis venenata following use of penicillin ointment \*384  
march dermatitis on chest and secondary and grease allergy of face, 68  
papular sarcoid of, 208  
papulonecrotic tuberculid including involvement of face, chest and back, 205
- Fat. See also Lipoids  
demonstration of effect of nutrition on skin, 401  
in Blood. See Blood, fats and lipoids
- Favre-Nicolas' Disease. See Lymphogranuloma Venereum
- Febricula. See Fever
- Feet. See Foot
- Felsher, Z. Cushing's syndrome 63  
Generalized progressive scleroderma with involvement of glottis and esophagus, 196  
Leukomelanoderma following arsenical dermatitis (malignant melanoma), 64
- Fetus. See Pregnancy
- Fever. See also Temperature, etc  
and sterile abscess formation accompanying treatment of syphilis with penicillin, \*399  
San Joaquin. See Coccidioidomycosis  
Therapeutic. See Impetigo contagiosa, Neurosyphilis, Syphilis, etc
- Fields R. J. Necrobiosis lipoidica diabetorum, 41
- Fifth Venereal Disease. See Granuloma inguinale
- Filariasis in Samoan area, 411
- Fingers and Toes. See also Foot, Hand
- Nails. See Nails  
recurrent erythema multiforme confined to 1 finger, 57
- Fluorescein. See Extremities, blood supply
- Folliculitis decalvans (Little) lichen planopilaris, lichen planus et acuminatus atrophicus (Feldman) and lichen spinulosus, 213  
keloidalis 123  
of extremities, pyoderma, perifolliculitis capitis abscedens et suffodiens, 212
- Food. See also Nutrition, Vitamins  
dried, dermatitis from dehydration of potatoes, \*9
- Foot. See also Fingers and Toes, etc  
arsenical keratoses of palms and soles or trophic ulcer of, 126  
sandals and hygiene and infections of feet \*365  
trench foot 186  
undeclared acid in treatment of dermatomycosis \*166
- Foreskin. See Penis
- Foster, P. D. Herpes simplex of buttocks, 54  
Seborrheic dermatitis, case for diagnosis, 55
- Fourth Venereal Disease. See Lymphogranuloma Venereum
- Fox H. American leishmaniasis 207  
Generalized progressive scleroderma, 123  
Pachyonychia congenita, 125  
Pityriasis rubra pilaris, 128
- Frambesia, treatment of yaws with penicillin, 407  
yaws, 37  
yaws in white soldier, 407
- Franklin, J. L. Creeping eruption, results of treatment with fuadin, \*174
- Franks A. G. Penicillin in treatment of cutaneous disease \*14
- Freeman H. E. Acute monocytic leukemia cutis (Naegely variety), 275  
Fixed bismuth dermatitis, case for diagnosis, 275  
Lichen planus with trophic lesion or lichen sclerosus et atrophicus of Hallopeau, 51  
Progressive pigmentary dermatosis (Schamberg's disease), case for diagnosis, 52
- Frei Reaction. See Lymphogranuloma Venereum
- Friderichsen-Waterhouse Syndrome. See Adrenals, hemorrhage
- Friedman R. Idiopathic gangrene of penis complicating scabies, 297  
Tuberculosis cutis (?) and psoriasis, 294
- Frontal Bone, congenital cyst of, 56
- Frost K. Erythema multiforme, case for diagnosis, 143  
Lupus erythematosus and psoriasis coexisting in same patient 53
- Fuadin. See Creeping Eruption
- Fuller J. R. New cutaneous bactericidal agent used in soap, further practical studies \*385

- Fungi See also *Aspergillus*, *Blastomycosis*, *Monilliasis*, *Mycosis*, *Ringworm*, *Trichophytosis*, etc  
alkaline medium and procedure for selection of dermatophytes in presence of saprophytic fungi, 410  
courses in mycology and radiologic physics, 269  
fungous infection of back of neck, 293  
improved method for preparing permanent slides of fungus cultures, \*267  
relation of ultraviolet-induced mutations to speciation in dermatophytes, \*257  
semblance of elastic tissue to mycelium in potassium hydroxide preparations, \*115, 401  
treatment of external otitis, local sulfonamide therapy, 272
- Fungicide See *Ringworm*
- Furunculosis, demonstration of effect of nutrition on skin, 401
- Fusospirochetosis, penicillin pastilles for oral infection, 412  
treatment of Vincent's angina with sulfathiazole, 407  
Vincent's disease of skin, \*87
- G-II See *Phenylmethane*
- Gammel, J A Systematized epithelial nevus, 421
- Gangrene, idiopathic, of penis complicating scabies, 297  
superficial, in adolescent diabetes, 187
- Gant, J Q, Jr One hundredth anniversary of first American textbook of dermatology, 117
- Gaumont *Xeroderma pigmentosum*, additional notes on 6 cases of Dr Mayrand and Dr Gaumont, \*176
- General Paralysis See *Dementia Paralytica*
- Genitals See under names of genitals, as *Penis*, etc
- German Measles See *Rubella*
- Germicides, new cutaneous bactericidal agent used in soap, further practical studies, \*385
- von Gierke's Disease See *Glycogen*
- Glichrist's Disease See *Blastomycosis*
- Gingivitis See *Fusospirochetosis*
- Glossitis See *Tongue*
- Glottis generalized progressive scleroderma with involvement of glottis and esophagus, 196
- Glycogen, hyperpigmentation of abdomen (von Gierke's disease, hyperinsulinism?), 61
- Goebel, M E Fever and sterile abscess formation accompanying treatment of syphilis with penicillin, \*399
- Goeckerman, W H Kendal Frost, 403  
*Lichen planus* or *lupus erythematosus*, 143
- Gold and Gold Compounds, *lupus erythematosus*, *psoriasis-rosea-like* dermatitis following therapy with gold salt, 193  
Therapy See *Purpura annularis telangiectodes*
- Goldberg, L C *Lupus erythematosus*, treatment with oxophenarsine hydrochloride, \*89  
Penicillin in treatment of cutaneous diseases, 184
- Goldstein, H I Use of methenamine in dermatology, 185
- Goldstein's Disease See *Telangiectasia*
- Goldzieher J W Adrenal glands in pemphigus vulgaris, report of 6 autopsies and review of literature, \*369
- Gordon, H H Treatment of ichthyosis, \*178
- Gordon Test See *Hodgkin's Disease*
- Gotttron's Disease See *Ichthyosis*
- Grace A W Fever and sterile abscess formation accompanying treatment of syphilis with penicillin, \*399
- Grafts See under *Skin*
- Graham, J C *Lupus pernio* (Besnier), 208
- Graham, T A Allergic eruption, case for diagnosis 425  
Purpura of unknown cause, 134
- Granuloma annulare 68 424  
annulare disseminated with atrophy 278  
annulare with discriminate lesions 278  
Coccidioid See *Coccidioidomycosis*
- Granuloma—Continued  
Fungoides See *Mycosis fungoides*  
infectious (tuberculous, syphilitic?), 210  
Inguinale, 49, 69, 410 See also *Lymphogranuloma Venereum*  
inguinale, amebic infection of vulva complicating granuloma pudendi, 273  
inguinale, experimental investigation of etiology and immunology, 406  
inguinale, failure of penicillin in treatment, report of case, \*182  
inguinale, polyarticular arthritis and osteomyelitis due to, 35  
inguinale, review of progress, 120  
Malignant See *Hodgkin's Disease*  
Paracoccidioid See *Blastomycosis*  
Tropicum See *Frambesia*  
Venereal See *Lymphogranuloma Venereum*
- Grease, match dermatitis on chest and secondary and grease allergy of face, 68
- Green, W S Semblance of elastic tissue to mycelium in potassium hydroxide preparations, \*115, comment by Pels, 401
- Gross, E Primary inoculation tuberculosis, 293
- Gumma See *Syphilis*, tertiary
- Gums, Diseases See *Fusospirochetosis*
- Habermann's Disease See *Pityriasis lichenoides et varioliformis acuta*
- Hair See also *Alopecia*  
Lacquer See *Cosmetics*  
pigmentation on transplanted skin in hooded rats, \*347  
trichophytosis barbae, 419
- Hall, A F Contact dermatitis due to pigment in zinc chromate primer, 279  
Contact dermatitis due to "Protek," 279  
Contact dermatitis due to resinous ingredients of zinc chromate primer and certain lacquers, 279  
Epithelioma of lip, case for diagnosis, 144
- Hallopeau's Disease See *Acrodermatitis*
- Halloran, C Late syphilis, case for diagnosis, 141
- Hand See also *Fingers and Toes*  
epithelial cysts, 410
- Hansen's Disease See *Leprosy*
- Haserick, J R Failure of penicillin in treatment of granuloma inguinale, report of case, \*182
- Hathaway, J C Vitamin B complex for vitiligo, 117
- Haxthausen's Disease See *Keratosis*
- Hazen, H H Extragenital syphilitic infection in Negroes, \*114  
Psoriasis, contact dermatitis, 47
- Headache, lumbar puncture headaches, 407
- Heart, white cross striae of finger nails following cardiac infarction, \*106
- Hecht, H Recurrent urticaria chronica, 424
- Hemophilus Ducreyi See *Chancroid*
- Hemorrhage See under *Adrenals*, etc  
Cutaneous See *Purpura*
- Henningsen, A B *Lupus vulgaris*, 194
- Heredity, relation of ultraviolet-induced mutations to speciation in dermatophytes, \*257
- Herpes, herpetic stomatitis in infants and children, 37  
psoriasis or vesicular lichen planus, 67  
simplex of buttocks, 54  
simplex resembling herpes zoster, 423  
use of methenamine in dermatology, 185  
zoster, chickenpox and acute anterior poliomyelitis, 410  
zoster, Hunt's syndrome, 62  
zoster, keloid following, 203  
zoster resembling herpes simplex, 423
- Hidradenitis See under *Sweat Glands*
- Hidradenoma, adenoma of apocrine sweat glands (hidradenoma) of anal canal, 120
- Histoplasmosis (Darling), 130
- Hodgkin's Disease 407  
with pruritus, 194

- Hollaender A Relation of ultraviolet induced mutations to speciation in dermatophytes, \*257
- Hormones See Adrenal Preparations, Androgens, Estrogens, Insulin, etc
- Hosiery See Clothing
- Hospitals, Army Air Forces dermatology program, \*6  
dermatologic practice in station hospital in Southern California, comparison with private practice, \*21  
dermatology in army station hospital serving in Italy, \*335
- Hubler W R Acrodermatitis atrophicans chronica with fibrous cutaneous nodules, 116  
Angloendothelioma of skin, 419  
Granuloma annulare, 424  
Sarcoid or late cutaneous syphilis 111  
Trichophytosis barbae 419  
Xeroderma pigmentosum with precocious malignancy, 421
- Hunt Syndrome See Herpes zoster
- Hutchinson-Bocock Sarcoid See Sarcoidosis
- Hydroa puerorum, atypical or achromic nevus 297
- Hyperergy See Anaphylaxis and Allergy
- Hyperhidrosis See Sweat Glands
- Hyperinsulinism See Insulin, Pancreas tumors
- Hyperkeratosis See Keratosis
- Hyperpigmentation See Pigmentation
- Hyperproteinemia See Blood, proteins
- Hyperpyrexia See under Syphilis, etc
- Hypohidrosis See Sweat Glands
- Hypothyroidism See Mixedema
- Hypotrichosis See Alopecia
- Ichthyosis, Ichthyosiform erythroderma 130  
or lichen planus hypertrophicus 137  
Simplex See Xeroderma  
treatment of \*178
- Icterus See Jaundice
- Immunity See Anaphylaxis and Allergy Antigens and Antibodies, etc
- Impetigo Bullosa in tropics \*28 268  
contagiosa, cured by fever, 37  
contagiosa treated with microcrystalline sulfathiazole 273
- Industrial Diseases See also Mines and Miners etc  
contact dermatitis due to pigment in zinc chromate primer, 279  
contact dermatitis due to 'Protek' 279  
contact dermatitis due to resinous ingredients of zinc chromate primer and certain lacquers 279  
dermatitis from dehydration of potatoes \*9  
light sensitization (in electric welder) 122  
lupus erythematosus of occupational origin 209  
occupational dermatitis caused by germicidal powder "Microlene," 407  
oil acne of unusual type, 144  
seborrheic dermatitis case for diagnosis 55  
skin hazards in manufacture and processing of synthetic rubber, 407
- Infantile Paralysis See Poliomyelitis
- Infants See also Children  
acute glomerular nephritis in infant with congenital syphilis 405  
calcinosis universalis in, 122  
"diaper rash" due to Perm-Aseptic 108  
hair lacquer dermatitis from contact with mother's hair, 272
- Infarction See Heart
- Infectious Diseases See Diphtheria, Syphilis, etc
- Injections, intensive treatment of early syphilis with oxophenarsine hydrochloride by multiple injections, \*155
- Inositol, role in alopecia of rats fed sulfasuxidine 36
- Instruments, contact dermatitis of eyelids caused by antioxidant in rubber fillers of eyelash curlers, report of 7 cases, \*262  
penetration of surface tissues with copper by iontophoresis, penetration with organic and inorganic copper salts and use of detergents in iontophoresis, \*96
- Insulin See also Diabetes Mellitus  
hyperpigmentation of abdomen (von Gierke's disease, hyperinsulinism?), 61
- Ion Transfer, penetration of surface tissues with copper by iontophoresis, penetration with organic and inorganic copper salts and use of detergents in iontophoresis, \*96
- Iontophoresis See Ion Transfer
- Irritation and carcinogenesis, 121
- Irring L Sandals and hygiene and infections of feet \*365
- Itching See Pruritus
- Ivy Poisoning See Rhus, poisoning
- Jacobson H P Nodular interstitial glossitis due to syphilis, 277
- Jadassohn's Disease See Atrophy
- Jaundice, post-arsphenamine, prevention of 412
- Jensen A K Blastomycosis or sporotrichosis 142  
Pellagra or pityriasis rubra pilaris 145
- Jericho Bell See Leishmaniasis
- Johnson H M Case for diagnosis 67  
Granuloma annulare 68  
Lichen nitidus 67  
Match dermatitis on chest and secondary and grease allergy of face 68  
Tuberculosis verrucosa cutis, 68  
Waterhouse Friderichsen syndrome report of case \*391
- Johnson-Stevens Disease See Erythema multiforme
- Joints See also under names of joints  
Diseases See Arthritis etc
- Juxta-Articular Nodes See Nodes
- Kagen M S Urticarial reaction from penicillin 291
- Kahn J B Urticaria from perfume \*11
- Kahn Test See under Syphilis
- Kala-azar See Leishmaniasis
- Kaposi's Disease See Xeroderma pigmentosum  
Sarcoma See Sarcoma  
Verruciform Frupion See Pyoderma
- Keddie, F M Histoplasmosis (Darling) 130
- Keloids See also Cicatrix  
folliculitis keloidalis 123  
following herpes zoster, 203
- Kennedy J V Xanthoma tuberosum, 45
- Keratoderma See Keratosis
- Keratosis See also Ichthyosis  
arsenical of palms and soles or trophic ulcer of foot 126  
blennorrhagica case for diagnosis 206  
disturbances of visual adaptation and their clinical significance, 36  
palmaris et plantaris 190  
porokeratosis 291  
psoriasis of palms and soles or keratoderma ciliatrum 123
- Kidneys Diseases See Nephritis  
systemic manifestations of bismuth toxicity, 405
- Kirby-Smith H Acute disseminated lupus erythematosus 42  
Mycosis fungoides, tumor stage 41
- Kittredge, H Amyloidosis cutis 19
- Koretshy, L Lupus vulgaris or sarcoid (Darier-Roussy), 178
- Korth Z N Case for diagnosis 47  
Dyskeratoid dermatosis, case for diagnosis, 46  
Kaposi's sarcoma or lichen planus hypertrophicus, 99
- Krause M I Dystrophic mediana canaliformis, 418  
Lupus vulgaris erythematosus of Leloir, case for diagnosis, 117
- Kussmaul-Maler Disease See Periarthritis nodosa
- Labia Majora See Vulva
- Lacquers, contact dermatitis due to resinous ingredients of zinc chromate primer and certain lacquers, 279
- Nail Lacquer See Cosmetics

- Ladany, E Dermatology in army station hospital serving in Italy, \*335
- Lamb I H Allergic reactions during administration of penicillin, \*93
- Lanc, C G John Harper Blaisdell, 119
- Vitiligo scleroderma or lichen sclerosus et atrophicus, 140
- LaRocco, C G Sarcoidosis, 414
- Larva Migrans See Creeping Eruption
- Lawrence, H Granuloma annulare, case for diagnosis, 68
- Laymon, C W Classification of tuberculosis of skin, \*108
- Lichen sclerosus et atrophicus in childhood, \*351
- Lederle-Vollmer Test See Tuberculosis
- Legs See also Extremities, Foot
- angiokeratoma of, 273
- Ulcers See Ulcers
- Lelomyoma, multiple, 218
- Leishmaniasis, American, 207
- cutaneous (oriental sore), treatment with quinacrine hydrochloride, \*26
- Lentz, J W Carbohydrate metabolism and skin, \*301
- Lepromin See Leprosy
- Leprosy, differentiation of lepromatous from "neural" leprosy, basis, method and report of 5 cases, \*354
- lepra maculoanesthetica, 290
- our leprosy problem, 411
- recent trends in United States, 407
- tuberculoid, sarcoidosis, late latent syphilis (treated), 413
- Leukemia, acute monocytic leukemia cutis (Naegely variety), 275
- cutis or mycosis fungoides, 54
- Leukocytes See Eosinophils, Leukemia, Lymphocytes, etc
- Leukoderma See Vitiligo
- Leukomelanoderma See Melanin, pigmentation
- Levin, O L Localized myxedema, 211
- Levine, B Folliculitis keloidalis, 423
- Herpes simplex resembling herpes zoster, 423
- Mycosis fungoides, 420
- Lewis G M Acrodermatitis continua or psoriasis, 204
- Calcinosis cutis or osteopetrosis, 128
- Dermatomyositis, psychoneurosis, dermatitis medicamentosa (pentobarbital sodium), cutis marmorata, 215
- Psoriasis of nails, case for diagnosis, 205
- Psoriasis of palms and soles or keratoderma climacterium, 123
- Recurrent erythema multiforme confined to 1 finger, 57
- Urticaria pigmentosa (acquired type), case for diagnosis, 209
- Lice See Pediculosis
- Lichen nitidus, 67, 141
- planopilaris, 188
- planopilaris lichen planus et acuminatus atrophicus (Feldman), lichen spinulosus and folliculitis decalvans (Little), 213
- planus atrophicus, 41
- planus et acuminatus atrophicus (Feldman), lichen planopilaris lichen spinulosus and folliculitis decalvans (Little), 213
- planus hypertrophicus or ichthyosis, 135
- planus hypertrophicus or Kaposi's sarcoma 39
- planus, lichenoid purpuric dermatitis (Gougerot and Blum), avitaminosis A or parapsoriasis, 139
- planus or lupus erythematosus 113
- planus or verruca plana, 192
- planus tropical lichen planus-like disease, \*1
- planus vesicular psoriasis or herpes 67
- planus with atrophic lesions or lichen sclerosus et atrophicus of Hallopeau 51
- sclerosus et atrophicus 142
- sclerosus et atrophicus in childhood \*351
- sclerosus et atrophicus of Hallopeau or lichen planus with atrophic lesions 51
- sclerosus et atrophicus or morphea, 61
- sclerosus et atrophicus vitiligo or scleroderma, 140
- Lichen—Continued
- scrofulosorum and tuberculosis colliquativa, 189
- scrofulosorum or lichen syphiliticus (extragenital infection), 195
- spinulosus, lichen planopilaris, lichen planus et acuminatus atrophicus (Feldman) and folliculitis decalvans (Little), 213
- spinulosus, psoriasis, pseudopelade (lichen spinulosus) and/or alopecia areata, 208
- striatus, 199
- syphiliticus (extragenital infection) or lichen scrofulosorum, 195
- verrucosus et reticularis (Kaposi), porokeratosis striata (Nekam), morbus moniliformis lichenoides (Wise and Rein), 129
- Lichenification See Neurodermatitis
- Lichens See Fungi
- Light See also Ultraviolet Rays, etc
- is penicillin a photosensitizing agent? \*17
- sensitization (in electric welder), 122
- xeroderma pigmentosum with precocious malignancy, 421
- Limbs See Arms, Extremities, Legs
- Lingua See Tongue
- Lipemia See Blood, fats and lipoids
- Lipids See Lipoids
- Lipoidosis See Xanthoma
- Lipoids, effect of feeding lipotropic substance to patients with xanthelasma, \*252
- in Blood See Blood, fats and lipoids
- necrobiosis lipoidica diabetorum, 41, 291
- necrobiosis lipoidica without diabetes, 295
- xanthoma or lipid disturbance, 295
- Lips, epithelioma, case for diagnosis, 144
- melanoma, case for diagnosis, 203
- Literature, one hundredth anniversary of first American textbook of dermatology, 117
- Little, R P Carbarsone in treatment of pemphigus, preliminary report, \*397
- Liver, acute yellow atrophy in early syphilis, case report with summary of literature, 120
- Therapy See Lupus erythematosus
- Loewenthal, K Sensitivity of tuberculin patch test (Vollmer-Lederle), results with 318 persons presenting various dermatoses, \*249
- Lonchocarpus, allergy from timbó (Lonchocarpus H B K), 409
- Lowenfish, F P Infectious granuloma (tuberculous, syphilitic), 210
- Luetin Test See under Syphilis
- Lumbar Puncture See Spinal Puncture
- Lungs, Tuberculosis See Tuberculosis, pulmonary
- Luotest See under Syphilis
- Lupoid See Sarcoidosis
- Lupus See also Tuberculosis
- erythematosus, 285
- erythematosus, acute disseminated, 42
- erythematosus and psoriasis coexisting in same patient, 53
- erythematosus, case for diagnosis, 196, 294
- erythematosus, discoid type, 50
- erythematosus hypertrophicus, 417
- erythematosus of occupational origin, 209
- erythematosus or lichen planus, 143
- erythematosus, pityriasis-rosea-like dermatitis following therapy with gold salt, 193
- erythematosus, possible, 128
- erythematosus profundus, case for diagnosis, 67
- erythematosus, treatment with oxophenarsine hydrochloride, \*89
- pernio (Besnier), 208
- vulgaris, 67, 192, 194, 288
- vulgaris erythematosus of Leloir, case for diagnosis 417
- vulgaris or sarcoid (Darier-Roussy), 138
- Lygranum See Lymphogranuloma Venereum
- Lymph Nodes See Leukemia, Lymphosarcoma, etc
- Lymphangitis chronic or rhinoscleroma, 57
- Tropical See Filariasis
- Lymphedema See Edema, hereditary
- Lymphoblastoma See also Hodgkin's Disease
- of scrotum 214

- Lymphocytes, role in antibody formation, 408
- Lymphogranuloma, Hodgkin's See Hodgkin's Disease
- Inguinale See Granuloma inguinale, Lymphogranuloma Venereum
- Schaumann's See Sarcoidosis
- Lymphogranuloma Venereum, discussion of some points related to, 274
- Lymphopathia Venerea See Lymphogranuloma Venereum
- Lymphosarcoma of nose, 287
- McCaleb, L Squamous cell epithelioma, case for diagnosis, 44
- McCauley, F J Henry J F Wallhauser, 270
- McClendon, J T Demonstration of effect of nutrition on skin, 401
- McCrae, L E Idiopathic gangrene of penis complicating scabies, 297
- McGuire, J A Fixed bullous eruption due to sulfathiazole, \*342
- Machacek, G T Psoriasis, pseudopelade (lichen spinulosus), and/or alopecia areata, 208
- Pyoderma, perfolliculitis capitis abscedens et suffodiens, folliculitis of extremities, 212
- Machlin, M T Xeroderma pigmentosum, additional notes on 6 cases of Dr Mayrand and Dr Gaumond, \*176
- MacVicar, D N Adenoma sebaceum (Pringle type forme fruste), 422
- Lupus erythematosus hypertrophicus, 117
- Scleroderma en coup de sabre, 420
- Maler-Kusssmaul Disease See Periarthritis nodosa
- Majocchi's Disease See Purpura annularis telangiectodes
- Mal del Pinto See Pinta
- Malformations See Abnormalities and Deformities
- Malnutrition See Nutrition, Vitamins, etc
- Mammary Gland See Breast
- Mantoux Reaction See Tuberculosis
- Mapharsen See Arsenic and Arsenic Compounds, Syphilis, etc
- Marble Bones See Osteosclerosis fragilis
- Markson, L S Dermatitis venenata following use of penicillin ointment, \*381
- Match dermatitis on chest and secondary and grease allergy of face, 68
- Mayrand xeroderma pigmentosum, additional notes on 6 cases of Dr Mayrand and Dr Gaumond, \*176
- Measles German See Rubella
- Medicine Aviation See Aviation and Aviators
- Military See Military Medicine
- Naval See Naval Medicine
- Tropical See Tropical Medicine
- Mehmert, H E Sandals and hygiene and infections of feet, \*365
- Meige's Disease See Edema hereditary
- Melanin See also Melanoma, Pigmentation
- pigmentation, leukomelanoderma following arsenical dermatitis (malignant melanoma), 64
- Melanoma, 69
- case for diagnosis, 203
- leukomelanoderma following arsenical dermatitis (malignant melanoma), 64
- Melanosis See Melanin, pigmentation
- Meningococci, Waterhouse-Friderichsen syndrome, report of case, \*391
- Menopause, psoriasis of palms and soles or keratoderma climacterium, 123
- Mental Diseases See Neuroses and Psychoneuroses
- Metasyphilis See Syphilis, congenital
- Methenamine, use in dermatology, 185
- Mibelli's Disease See Angiokeratoma
- Michelson, H E Classification of tuberculosis of skin, \*108
- Epidermolysis bullosa, case for diagnosis 285
- Lupus erythematosus 285
- Mycosis fungoides 286
- Periarthritis nodosa, 292
- Microfilaria See Filariasis
- Microleone See Dermatitis venenata
- Microsporosis, erythrasma in South Pacific, \*75
- Military Medicine See also Aviation and Aviators, Gas, etc
- clinical investigation of new cutaneous entity, \*226
- cutaneous diseases in South Pacific, observations among military forces, \*75
- dermatologic practice in station hospital in Southern California, comparison with private practice, \*21
- dermatology in army station hospital serving in Italy, \*335
- effective 3 hour treatment of scabies, 184
- filariasis in Samoan area, 411
- medical experiences in North Africa 1943 4, 187
- new cutaneous syndrome occurring in New Guinea and adjacent islands, preliminary report, \*221
- sandals and hygiene and infections of feet, \*365
- skin diseases in tropics, 37
- skin diseases with army in India, 122
- staining of skin from quinaerine hydrochloride, case for diagnosis, 199
- treatment of ichthyosis, \*173
- trench foot 186
- tropical anhidrotic asthenia, 37
- war and oxygen therapy, 410
- jaws in white soldier, 407
- Millum, Colloid See under Skin
- Miller, H E Lichen verrucosus et reticularis (Kaposi), porokeratosis striata (Nekâm), morbus moniliformis lichenoides (Wise and Rein), 129
- Miller, J L Alopecia areata or arsenical dermatitis, 426
- Parapsoriasis or secondary syphilis, 213
- Pediculosis of eyelashes, 427
- Psoriasis, 427
- Recurrent syphilis, macular atrophy secondary to syphilis 212
- Sarcoid, 427
- Millroy's Disease See Edema, hereditary
- Mines and Miners factors influencing dermatitis in coal miners, 187
- Mitchell, J H Acrodermatitis, case for diagnosis, 288
- Lichen sclerosus et atrophicus or morphea, 61
- Neurotic excoriations, case for diagnosis, 65
- Staining of skin from quinaerine hydrochloride, case for diagnosis, 199
- Molds See Fungi
- Moles See Neri
- Moniliasis or congenital ectodermal defect, 194
- generalized, and trichophytosis, 277
- generalized cutaneous monilial infection 272
- lichen verrucosus et reticularis (Kaposi) porokeratosis striata (Nekâm), morbus moniliformis lichenoides (Wise and Rein), 129
- Montenegro Test See Leishmaniasis
- Montgomery, R M Lupus vulgaris, 192
- Tinea ciliarum and tinea corporis, 426
- Morphea See Scleroderma
- Morris, G E Neurodermatitis circumscripta or dermatitis factitia, 138
- Mouth See also Stomatitis, etc
- dermatologic diseases frequently encountered by otolaryngologists, 410
- penicillin pastilles for oral infection 412
- Mozart, erythema nodosum in 18th century, case of child Mozart 33
- Mucous Membrane See also Lips, Mouth Nose, etc
- erythema multiforme, report of case of severe erythema multiforme with involvement of mucous membranes treated with penicillin \*91
- Muskatbitt, E Ringworm of eyebrow \*116
- Semblance of elastic tissue to mycellum in potassium hydroxide preparations 401 [comment on article by Green and Shepard]
- Mutation See Heredity
- Mycellum, semblance of elastic tissue to mycellum in potassium hydroxide preparations \*115 401
- Mycobacterium Lepae See under Leprosy
- Mycology See Fungi, Mycosis



- Mycosis** See also Blastomycosis, Monilliasis, Ring-worm, Tinea, etc  
cutaneous, in South Pacific, \*75  
cutaneous, onychomycosis and dermatomycosis caused by *Trichophyton rubrum* and *Aspergillus nidulans*, \*162  
cutaneous, skin diseases with army in India, 122  
cutaneous undecylenic acid in treatment of dermatomycosis, \*166  
fungoides, 48, 58, 286, 420, correction, 185  
fungoides, acrodermatitis atrophicans chronica with fibrous cutaneous nodules, 416  
fungoides exhibiting large concentric lesions and treated with testosterone, 298  
fungoides in Negro, \*18, 63  
fungoides or leukemia cutis, 54  
fungoides, premycosis fungoides, 287  
fungoides, tumor stage, 44  
**Mixedema**, localized, 211
- Nails**, abnormalities, pachyonychia congenita, 125  
*dystrophia mediana canaliformis*, 418  
onychomycosis due to *Trichophyton purpureum*, 124  
onychomycosis and dermatomycosis caused by *Trichophyton rubrum* and *Aspergillus nidulans*, \*162  
psoriasis of, case for diagnosis, 205  
undecylenic acid in treatment of dermatomycosis, \*166  
white cross striae of finger nails following cardiac infarction, \*106
- Nares** See Nose
- Naval Medicine** See also Aviation and Airliners, Hospitals, Military Medicine, etc  
cutaneous diseases in South Pacific, observations among military forces, \*75  
salt water ulcers of extremities, occurrence in Japanese survivors, 411
- Navies** See Naval Medicine
- Neck**, fungous infection of back of, 293
- Necrobiosis Lipoidica** See Skin, diseases
- Necrosis** See Roentgen Rays
- Negroes** esophageal carcinoma in British West Indian and Panamanian Negroes, study of incidence, etiologic factors and pathologic anatomy in 50 cases, 406  
extragenital syphilitic infection in, \*114  
mycosis fungoides in, \*18, 63
- Neosphenamine** See Arsphenamines and under names of various diseases as Syphilis, etc
- Neoplasms** See Cancer, Sarcoma
- Nephritis** acute glomerular, in infant with congenital syphilis, 405
- Nerves**, differentiation of lepromatous from "neural" leprosy, basis, method and report of 5 cases, \*354  
optic, neurosyphilis and oculist, 121
- Nervous System**, Syphilis See Neurosyphilis
- Netherton, F W** Acrodermatitis atrophicans chronica with fibrous cutaneous nodules, 416  
Angioendothelioma of skin, 419  
Granuloma annulare, 424  
Sarcoid or late cutaneous syphilis, 414  
Trichophytosis barbae, 419  
Xeroderma pigmentosum with precocious malignancy, 421
- Neurodermatitis circumscripta** or dermatitis factitia, 138
- Neurofibromatosis** multiple, of peculiar papular form, 283  
von Recklinghausen's disease, 62  
von Recklinghausen's disease in identical twins, 212
- Neuroma** cutaneous, 202
- Neuroses and Psychoneuroses**, dermatomyositis, psychocutis, dermatitis medicamentosa (pentobarbital sodium), cutis marmorata, 215  
rescue excretions, case for diagnosis, 65  
rescue excretions or dermatitis factitia, 137
- Neurosyphilis** See also Dementia Paralytica, Tabes D. Sals  
\*12 oculist, 121  
\*12 oculist, 122  
\*12 oculist, 123
- Nevi** See also Angioma  
achromic, or atypical hydra puerorum, 297  
acne vulgaris occurring in tropics in pigmentary and pilosebaceous nevus, \*322  
angiokeratoma (unilateral nevus), 128  
comedonicus, 215  
linearis, case for diagnosis, 141  
nevus flammeus associated with conjunctival telangiectasia and possible early choroidal tumor, 35  
pigmentosus et pilosus, 202, 214  
systematized epithelial nevus, 421  
Vascular See Angioma, Telangiectasia
- Newhall, C A** New cutaneous bactericidal agent used in soap, further practical studies, \*385
- Nickerson, W J** Sandals and hygiene and infections of feet, \*365
- Nicolas-Favre Disease** See Lymphogranuloma Venereum
- Nicotinic Acid** See also Vitamins, B  
bacterial destruction of, 409
- Niedelman, M L** Pemphigus vulgaris improved by acetarsone, 298
- Nipples** See Breast
- Nisbet, T W** New cutaneous syndrome occurring in New Guinea and adjacent islands, preliminary report, \*221
- Nitritoid Reaction** See Arsenic and Arsenic Compounds
- Nodes** See also Erythema nodosum, etc  
acrodermatitis atrophicans chronica with fibrous cutaneous nodules, 416  
syphilitic joint-articular nodules combined with leukoderma of wrists, palms and feet, 66
- Nose**, chronic lymphangitis or rhinoscleroma, 57  
lymphosarcoma of, 287  
melanoma, 69  
rosacea and rhinophyma (nose and ear lobes), 201
- Nutrition** See also Vitamins, etc  
demonstration of effect on skin, 401
- Obermayer, M E** Multiple neurofibromatosis of peculiar papular form, 283  
Synovial pseudocysts, case for diagnosis, 52
- OBITUARIES**  
Blaisdell, John Harper, 119  
Buschke, Abraham, 32  
Frost, Kendal P., 269, 403  
Hopkins, Ralph, 30  
Wallhauser, Henry J F., 71, 270  
Wayson, James Thomas, 183
- Occupational Diseases** See Industrial Diseases
- Odors**, urticaria from perfume, \*11
- Oil** acne of unusual type 144  
Sulfonated See Detergents
- Ointments** See also Skin, diseases  
penicillin in treatment of cutaneous diseases, 184  
penicillin, studies on stability relative to potency and on sensitivity of human skin to patch tests with ointment, \*216  
propionate and undecylenate ointments in treatment of tinea pedis and in vitro comparison of their fungistatic and antibacterial effects with other ointments, 406
- Oleoresin** See Rhus, poisoning
- Oliver, E A** Dermatofibrosarcoma protuberans with dementia paralytica tabetic type 202
- Omens, D V** Hunt's syndrome, 62  
Lupus vulgaris, 288  
Pemphigus vulgaris, 200  
Systemic blastomycosis, 198  
Urticarial reaction from penicillin, 291
- Omens, H D** Hunt's syndrome, 62  
Lupus vulgaris, 288  
Pemphigus vulgaris, 200  
Systemic blastomycosis, 198
- Onychia** See Nails
- Onychodystrophy** See Nails
- Onychomycosis** See Nails

- Oppenheim M. Effective 3 hour treatment of scabies, 184  
 Necrobiosis lipoidica diabetorum, 291  
 Tuberculosis miliaris disseminata faciei, 59
- Optic Disk See Nerves, optic
- Oriental Sore See Ichthyomiasis
- Orman J M. Epidermolysis bullosa, suggestion as to possible causation \*317
- Ormsby O S. Pityriasis rubra pilaris (vitamin A deficiency), 201
- Osler's Disease See Telangiectasia
- Osmys See Odors
- Osteomyelitis and polyarticular arthritis due to granuloma inguinale, 35
- Osteopokkiosis See Osteosclerosis fragilis
- Osteosclerosis fragilis, calcinosis cutis or osteopokkiosis, 128
- Otsuka M. Blastomycosis, 62  
 Lepa maculoanesthetica, 290  
 Mycosis fungoides in Negro, 63  
 Pemphigus vulgaris, 200  
 Tubercloid, case for diagnosis, 197  
 Urticarial reaction from penicillin, 291  
 von Recklinghausen's disease, 62
- Owens B B. Beta dimethylaminoethyl benzhydryl ether hydrochloride (Benadryl) in treatment of urticaria, \*239
- Oxophenarsine Hydrochloride See Lupus erythematosus, Syphilis
- Oxygen therapy and war, 410
- Pachyonychia See Nails abnormalities
- Palate gumma of 69
- Pancratic tumors hyperpigmentation of abdomen (von Gierke's disease, hyperinsulinism?), 61
- Papilla Optic See Nerves optic
- Papilloma virus papillomas in burn scars, case for diagnosis, 66
- Paraffinoma, 42
- Paralysis See Poliomyelitis, etc  
 General See Dementia Paralytica  
 Infantile See Poliomyelitis
- Parapsoriasis, 288  
 and pulmonary tuberculosis 45  
 case for diagnosis 284  
 lichen planus, lichenoid purpuric dermatitis (Gougerot and Blum) or vitaminosis A, 139  
 lichenoides (Brocq) case for diagnosis, 140  
 or secondary syphilis 213  
 pityriasis lichenoides et varioliformis acuta, 136  
 288
- Paresis See Dementia Paralytica
- Pasteurella Tularensis See Tularemia
- Patch Test See Anaphylaxis and Allergy
- Peck S M. Dermatitis from dehydration of potatoes \*9
- Pediculosis of eyelashes, 427
- Pelada See Alopecia areata
- Pellagra or pityriasis rubra pilaris, 145
- Pels I R. Semblance of elastic tissue to mycellum in potassium hydroxide preparations 401 [comment on article by Green and Shepard]
- Pemphigus carbarsone in treatment, preliminary report \*397  
 case for diagnosis 60 218  
 erythematosis (Senear-Usher syndrome) or pemphigus vulgaris, 131  
 foliaceus Brazilian clinical concept of 188  
 or dermatitis herpetiformis, 200  
 vulgaris, 200  
 vulgaris adrenal glands in, report of 6 autopsies and review of literature \*369  
 vulgaris improved by acetarsone, 298  
 vulgaris or pemphigus erythematosis (Senear-Usher syndrome), 131
- Penicillin allergic reactions during administration of \*93  
 dermatitis venenata following use of ointment, \*384  
 experiments on toxicity of calcium salt of penicillin 36  
 fever and sterile abscess formation accompanying treatment of syphilis with penicillin \*399
- Penicillin—Continued  
 in civilian practice, 412  
 is penicillin a photosensitizing agent? \*17  
 ointment, studies on stability relative to potency and on sensitivity of human skin to patch tests with ointment, \*216  
 Therapy See Anthrax, Coccioidomycosis, Erysipeloid, Erythema multiforme, Frambesia Granuloma inguinale, Skin, diseases, Syphilis, etc  
 urticarial reaction from, 291
- Penis, Bowen's disease of, late latent syphilis (treated), 413  
 idiopathic gangrene of penis complicating scabies 297
- Pentobarbital See Barbitol and Barbitol Derivatives
- Pereyra A J. Penetration of surface tissues with copper by iontophoresis, penetration with organic and inorganic copper salts and use of detergents in iontophoresis, \*96
- Perfume See Cosmetics
- Periarthritis nodosa, 292  
 nodosa, case for diagnosis, 422  
 nodosa of Kussmaul-Maier, 38  
 nodosa or vasculitis, 131
- Perifolliculitis capitis abscedens et suffodiens, pyoderma, folliculitis of extremities 212
- Periphelebitis perivascularitis nodularis necroticans or erythema induratum of unusual type, 133
- Perivascularitis See Periphelebitis
- Perm-Aseptic See Dermatitis venenata
- Perspiration See under Sweat Glands
- Phakomatosis See Sclerosis tuberosa
- Phalanges See Fingers and Toes
- Phemeride See Ammonia and Ammonium Compounds
- Phenol See Ringworm
- Phenolphthalein and Phenolphthalein Derivatives erythema perstans, 39
- Phenyl-Beta-Naphthylamine contact dermatitis of eyelids caused by antioxidant in rubber fillers of eyelash curlers report of 7 cases, \*262
- Phenylmethane new cutaneous bactericidal agent (G-11) used in soap, further practical studies \*385
- Phlebitis cutaneous and subcutaneous lesions of lower limbs in connection with veins, differential diagnosis, \*376
- Photosensitization See Light
- Phthirus Pubis See Pediculosis
- Phthisis See Tuberculosis pulmonary
- Physicians See Obituaries, etc
- Physics courses in mycology and radiologic physics, 269
- Pigmentation See also Hair, Melanin, Nevi, Schamberg's Disease, Xeroderma pigmentosum etc  
 hyperpigmentation of abdomen (von Gierke's disease, hyperinsulinism?) 61  
 staining of skin from quinacrine hydrochloride 199
- Pinta, postsyphilitic dyschromia late dyschromic pinta (treated), 415  
 White See Vitiligo
- Pirquet Reaction See under Tuberculosis
- Pityriasis Lichenoides See Parapsoriasis  
 rosea lupus erythematosus, pityriasis-rosea-like dermatitis following therapy with gold salt 193  
 rosea treatment with Trichophyton extract, 184  
 rubra pilaris 128, 137  
 rubra pilaris or pellagra, 145  
 rubra pilaris (vitamin A deficiency), 201  
 Versicolor See Tinea versicolor
- Plants See Rhus etc
- Plastics See Resins
- Poison Ivy See Rhus, poisoning
- Poisons and Poisoning See under names of substances
- Poliomyelitis acute anterior chickenpox and herpes zoster, 410

- Polyarteritis Nodosa** See *Periarteritis nodosa*
- Polycythemia, dermatitis medicamentosa** associated with secondary polycythemia, report of case, \*389
- with unusual eruption, \*172
- Popper, M** *Xanthelasma papulosum multiplex*, case for diagnosis, 51
- Poridontitis** See *Lymphogranuloma Venereum*
- Porokeratosis** See *Keratosis*
- Port Wine Mark** See *Nevi flammeus*
- Potassium hydroxide**, semblance of elastic tissue to mycelium in potassium hydroxide preparations, \*115, 401
- Potatoes**, dermatitis from dehydration of, \*9
- Pratt, A G** Generalized calcinosis cutis without involvement of muscles or nerves, 189
- Urticaria pigmentosa* with sensitiveness to temperature, 190
- Pregnancy**, rubella and congenital malformations, 407
- Prepuce** See *Penis*
- Pringle's Disease** See *Sebaceous Glands*
- Pringle-Bourneville's Disease** See *Sclerosis, tuberosus*
- Printz D R** Congenital ectodermal defect, 418
- Periarteritis nodosa*, case for diagnosis, 422
- Procline dermatitis medicamentosa** associated with secondary polycythemia, report of case, \*389
- Propionate** See *Ringworm*
- Proteins in Blood** See *Blood, proteins*
- Protek** See *Dermatitis venenata*
- Pruritus** with Hodgkin's disease, 194
- Pseudopelade** See *Alopecia cicatricata*
- Psoriasis**, 427
- and lupus erythematosus coexisting in same patient, 53
- and synovial cyst, 286
- and tuberculosis cutis, 294
- contact dermatitis, 47
- of nails, case for diagnosis, 205
- of palms and soles or keratoderma climacterium, 123
- or acrodermatitis continua, 204
- pseudopelade (lichen spinulosus) and/or alopecia areata, 208
- stimulating stasis dermatitis, 65
- vesicular lichen planus or herpes, 67
- Psychoneuroses** See *Neuroses and Psychoneuroses*
- Psychoses** See *Neuroses and Psychoneuroses*
- Purpura annularis telangiectodes (Majocchi)**, case for diagnosis 66
- annularis telangiectodes (Majocchi's disease?)* treated successfully with gold sodium thio-sulfate, 216
- of unknown cause, 134
- Waterhouse-Friderichsen syndrome**, report of case, \*391
- Pyoderma faciale** following dermatitis venenata, 215
- gangrenosum* associated with nonspecific ulcerative colitis, 416
- generalized vaccinia in eczematous child, demonstration of virus and comment on "Kaposi's varicelliform eruption," 405
- perifolliculitis capitis abscedens et sufficiens, folliculitis of extremities, 212
- Pyrethrum** See *Pediculosis, Scabies*
- Pyrocatechol**, relation of chemical structure in catechol compounds and derivatives to poison ivy hypersensitiveness in man as shown by patch test 35
- Quinacrine** See also *Acridine Dyes, Leishmaniasis*
- etc
- hydrochloride staining of skin from 199
- trichial lichen planus-like disease \*1
- Races** See *Negroes, etc.*
- Rachitic rickets** See *Spinal Puncture*
- Radiation** See *Poentgen Rays, Ultra-violet Rays*
- Radiation** See under *Poentgen Rays*
- Rattner, H** Course in tropical dermatology, 268
- Lupus erythematosus*, case for diagnosis, 196
- Melanoma*, case for diagnosis, 203
- Multiple superficial epitheliomatosis*, 289
- Parapsoriasis*, 288
- Pemphigus fungoides*, 287
- von Recklinghausen's Disease** See *Neurofibromatosis*
- Recruits** See *Military Medicine*
- Refraction** See *Eyes, accommodation and refraction*
- Reidu-Osler-Weber Syndrome** See *Telangiectasia*
- Resins**, dehydration in histologic embedding eliminated by use of water-soluble synthetic plastic, 120
- Reticuloendothelial System** See *Jaundice, Liver, etc.*
- Reyes, I G** *Epidermodysplasia hystricoidis bullosa*, report of case with histopathologic study, \*328
- Rhinophyma and rosacea** (nose and ear lobes), 201
- Rhinoscleroma** or chronic lymphangitis, 57
- Rhus**, poisoning, relation of chemical structure in catechol compounds and derivatives to poison ivy hypersensitiveness in man as shown by patch test, 35
- poisoning, status of poison ivy extracts, 408
- Ringworm** See also *Favus, Microsporiasis, Mycosis, cutaneous, Tinea, Trichophytosis, etc.*
- adjuvant effect of aerosol on germicidal action of cadmium chloride, 36
- cotton hose as vehicle for fungicide in treatment of athlete's foot, 36
- of eyebrow, \*116
- onychomycosis* and *dermatomycosis* caused by *Trichophyton rubrum* and *Aspergillus nidulans*, \*162
- phenol-camphor treatment of dermatophytosis, 273
- propionate and undecylenate ointments in treatment of tinea pedis and in vitro comparison of their fungistatic and antibacterial effects with other ointments, 406
- undecylenic acid in treatment of dermatomycosis, \*166
- Ritter's Disease** See *Dermatitis exfoliativa*
- Robinson, H C** *Erythema multiforme*, report of case of severe erythema multiforme with involvement of mucous membranes treated with penicillin, \*91
- Robinson, M M** Rosacea-like tuberculid of Lewandowsky or rosacea, 44
- Robinson S S** Colloid degeneration of skin (colloid milium), report of case, with observations on ascorbic acid therapy, \*180
- Dermatitis medicamentosa* associated with secondary polycythemia, report of case, \*389
- Roentgen Rays, Therapy** See under names of organs regions and diseases, as *Epithelioma, Sarcoma, etc.*
- treatment of post-irradiation necrosis, 410
- Roll, H C** *Pemphigus* or dermatitis herpetiformis, 200
- Romano, D** Penicillin in treatment of cutaneous disease, \*14
- Rony, H R** Effect of endocrine substances on adult human scalp, \*323
- Rosen I** Inoculation tuberculosis, 132
- Multiple leiomyoma*, 218
- Rosenbach Disease** See *Erysipeloid*
- Rothman, S** *Acanthosis nigricans*, juvenile type, 59
- Adenoma sebaceum (Pringle?)*, 195
- Bowen's disease*, 289
- Cushing's syndrome*, 63
- Erythema nodosum* in eighteenth century, case of child Mozart, 33
- Generalized progressive scleroderma with involvement of glottis and esophagus, 196
- Leukomelanoderma* following arsenical dermatitis (malignant melanoma), 64
- Undecylenic acid in treatment of dermatomycosis, \*166
- Rubber contact dermatitis** of eyelids caused by antioxidant in rubber fillers of eyelash curlers report of 7 cases, \*262
- Rubber Industry**, skin hazards in manufacture and processing of synthetic rubber, 467

- Rubella and congenital malformations, 407  
 Rubin, S S Impetigo bullosa in tropics, 268  
 Rullson, R H Chronic recurrent papulopustular dermatitis related to vitamin deficiency, 127  
 Lupus erythematosus of occupational origin, 209
- Sandals See Shoes
- Sarcoidosis, 413, 414  
 lupus vulgaris or sarcoid (Darier-Housay), 178  
 of Boeck metabolic studies of 3 cases, 105  
 papular sarcoid of face, 208  
 sarcoid, 112, 427  
 sarcoid, late secondary syphilis 218  
 sarcoid or late cutaneous syphilis 114  
 tuberculous leprosy, late latent syphilis (treated), 413
- Sarcoma See also Cancer, and under names of tumor, as Angiosarcoma, Dermatofibrosarcoma, Lymphosarcoma, etc  
 direct current combined with x-ray therapy, case of Kaposi sarcoma thus treated 187  
 Kaposi's or lichen planus hypertrophicus, 79
- Scabies, effective 3 hour treatment, 181  
 idiosyncratic kangrene of penis complicating scabies, 297  
 skin diseases with army in India, 122
- Scalp Diseases See under names of diseases as Ringworm Seborrhea, etc  
 effect of endocrine substances on adult human scalp, \*323  
 epithelioma probably arising from sweat glands 43
- Scars See Cicatrix
- Schamberg's Disease, progressive pigmentary dermatosis, 52 295
- Schaumann's Disease See Sarcoidosis
- Scheer, M Lymphoblastoma of scrotum 214
- Schuldkraut J M Juvenile xanthomatosis, 191
- Schmidt F R Treatment of dermatoses with vaso dilators, \*344
- Schmidt O F L Pemphigus vulgaris or pemphigus erythematosus (Sencar-Usher syndrome), 131
- Schmitt C L Clinical investigation of new cutaneous entity, \*226
- Scholtz J R Army Air Forces dermatology program, \*6
- Schorr, H C Congenital ectodermal defect or monilia 194  
 Dermatitis herpetiformis treated with acetarsone 292  
 Hyperpigmentation of abdomen (von Gierke's disease hyperinsulinism?), 61  
 Psoriasis simulating stasis dermatitis 65  
 Seborrheic dermatitis case for diagnosis 61
- Schwartz, G Pityriasis rubra pilaris 137
- Sclerodema See Scleroderma
- Sclerema See Scleroderma
- Sclerodactylia See Scleroderma
- Scleroderma, 44  
 and acrosclerosis, 56  
 on coup de sabre, 420  
 generalized progressive 123  
 generalized progressive with involvement of glottis and esophagus, 196  
 generalized progressive, with nodules, 210  
 lichen sclerosus et atrophicus or morphea, 61  
 morphea, case for diagnosis, 139  
 vitiligo or lichen sclerosus et atrophicus, 140
- Scleroma See Rhinoscleroma
- Serofula See Tuberculosis
- Scrotum lymphoblastoma of, 214
- Seull, R H Acrodermatitis, case for diagnosis 288  
 Lichen sclerosus et atrophicus or morphea, 61  
 Neurotic excoriations, case for diagnosis, 65
- Sebaceous Glands, acne vulgaris occurring in tropics in pigmentary and pilosebaceous nevus \*322  
 adenoma sebaceum, 282  
 adenoma sebaceum (Pringle?) 195  
 adenoma sebaceum (Pringle type forme fruste), 422  
 effect of endocrine substances on adult human scalp \*323
- Seborrhea, seborrheic dermatitis, case for diagnosis 55, 64, 287  
 tinea amiantacea, 145
- Section on Dermatology and Syphilology, American Medical Association, 429
- Sencar, F E Cutaneous neuroma, 202  
 Lichen striatus, 199  
 Pemphigus or dermatitis herpetiformis, 200  
 Rosacea and rhinophyma (nose and ear lobes), 201
- Sencar-Usher Syndrome See Pemphigus
- Septum, Nasal See under Nose
- Serum See Blood
- Shaffer B Fixed bullous eruption due to sulfathiazole, \*342
- Shaffer L W Intensive arsenotherapy of early syphilis, \*147  
 Use of Benadryl for urticaria and related dermatoses, preliminary report, \*243
- Shapiro, A L Acanthosis nigricans, juvenile type, 59  
 Adenoma sebaceum (Pringle?), 195  
 Bowen's disease, 289  
 Colloidoclastic shock following injection of oxophenarsine hydrochloride (mapharsen), report of case \*335  
 Undecylenic acid in treatment of dermatomycosis, \*166
- Shepard M C Semblance of elastic tissue to mycelium in potassium hydroxide preparations, \*115, comment 401
- Shipwrecks, salt water ulcers of extremities, occurrence in Japanese survivors, 411
- Shock Anaphylactic See Anaphylaxis and Allergy  
 Colloidoclastic See Anaphylaxis and Allergy
- Shoes, sandals and hygiene and infections of feet, \*365
- Sigel, H Mycosis fungoides in Negro \*18
- Silverman, M Granuloma inguinale, 69  
 Gumma of palate, 69  
 Melanoma, 69  
 Vasomotor dysfunction associated with hypohidrosis, 69
- Skin See also Dermatology  
 Abnormalities See also Atrophy, Ectodermal Defect, Pigmentation, etc  
 abnormalities dyskeratoid dermatosis, case for diagnosis 46  
 acrodermatitis atrophicans chronic with fibrous cutaneous nodules, 416  
 and carbohydrate metabolism, \*301  
 Atrophy See Atrophy  
 Cancer See Cancer, Epithelioma Sarcoma, etc  
 colloid degeneration (colloid miffum) report of case, with observations on ascorbic acid therapy, \*289  
 cutaneous and subcutaneous lesions of lower limbs in connection with veins, differential diagnosis, \*376  
 cutaneous neuroma 202  
 demonstration of effect of nutrition on, 401  
 dermatologic diseases frequently encountered by otolaryngologists, 410  
 dermatomyositis, psychoneurosis, dermatitis medicamentosa (pentobarbital sodium), cutis marmorata, 215  
 Diphtheria See under Diphtheria  
 Diseases See also Dermatitis, and under names of diseases, as Eczema, Herpes, Mycosis, etc, and under names of plants and drugs, as Penicillin, Rhus, etc  
 diseases among the natives of northeast New Guinea, \*247  
 diseases, Army Air Forces dermatology program, \*6  
 diseases, clinical investigation of new cutaneous entity, \*226  
 diseases, dermatologic practice in station hospital in Southern California, comparison with private practice, \*21  
 diseases, dermatology in army station hospital serving in Italy \*335  
 diseases in South Pacific, observations among military forces \*75  
 diseases in tropics 37  
 diseases, medical experiences in North Africa 1943-4 137

- Skin—Continued
- diseases, necrobiosis lipoidica diabetorum, 41, 291
  - diseases, necrobiosis lipoidica without diabetes, 295
  - diseases, overtreatment dermatitis, 408
  - diseases, penicillin in treatment of cutaneous disease, \*14, 184
  - diseases, sensitivity of tuberculin patch test (Vollmer-Lederle), results with 318 persons presenting various dermatoses, \*249
  - diseases, skin eruptions due to local application of sulfonamides, 411
  - diseases, treatment of dermatoses with vasodilators, \*344
  - diseases, use of methenamine in dermatology, 185
  - diseases with army in India, 122
  - effect of 3,4-benzpyrene on regenerating epidermis of mice, 35
  - Gangrene See Gangrene
  - Hemorrhage See Purpura
  - Inflammation See Dermatitis
  - new cutaneous bactericidal agent used in soap, further practical studies, \*385
  - new cutaneous syndrome occurring in New Guinea and adjacent islands, preliminary report, \*221
  - penicillin in civilian practice, 412
  - Pigmentation See under Pigmentation
  - principles of percutaneous absorption, 35
  - semblance of elastic tissue to mycelium in potassium hydroxide preparations, \*115, 401
  - staining from quinacrine hydrochloride, 199
  - Syphilis See Syphilis
  - transplantation, pigmentation of hair on transplanted skin in hooded rats, \*347
  - Tuberculosis See Tuberculosis
  - Tumors See under Tumors
  - Ulcers See Ulcers
  - Vincent's disease of, \*87
- Smallpox death caused by vaccinia in eczematoid infant, 186
- generalized vaccinia in eczematous child demonstration of virus and comment on "Kaposi's varicelliform eruption" 405
  - laboratory test for diagnosis of, 188
- Smith, E M, Jr Seborrheic dermatitis, case for diagnosis, 287
- Soaps See also Detergents
- new cutaneous bactericidal agent (G-11) used in soap, further practical studies, \*385
- Sobisminol See Syphilis
- Societies, dermatologic, directory of, 72, 430
- foreign, directory of, 72, 430
  - international, directory of, 72, 430
  - local, directory of, 73, 431
  - national, directory of, 72, 430
  - sectional, directory of, 72, 430
  - state, directory of, 72, 430
- SOCIETY TRANSACTIONS
- Atlantic Dermatologic Conference, 39
  - Central States Dermatological Society 413
  - Chicago Dermatological Society, 59 194, 287
  - Cleveland Dermatological Society, 423
  - Hawaii Dermatological Society, 66
  - Los Angeles Dermatological Society 50 141 275
  - Manhattan Dermatologic Society, 56, 132, 214
  - Metropolitan Dermatological Society, 192, 425
  - Minnesota Dermatological Society, 283
  - New England Dermatological Society, 136
  - New York Academy of Medicine Section of Dermatology and Syphilis 210
  - New York Dermatological Society, 123 203
  - Philadelphia Dermatological Society 189 293
  - San Francisco Dermatological Society, 129
- Sober effect of feeding lipotropic substance to patients with xanthelasma, \*252
- Specimens dehydration in histologic embedding eliminated by use of water-soluble synthetic plastic 120
- improved method for preparing permanent slides of fungus cultures \*267
- Stefel L Lichen planophyllis lichen planus et acuminatus atrophicans (Feldman) and lichen atrophicans and folliculitis decalvans (Little), 211
- Stout K Multiple neurofibromatosis of peculiar papular form, 283
- Strakosch, E A Lichen syphiliticus (extragenital infection) or lichen scrofulosorum, 195
- Strauch, J Bowen's disease of penis, late latent syphilis (treated), 413
- Postsyphilitic dyschromia, late dyschromic pinta (treated), 415
  - Sarcoidosis, 413
  - Sarcoidosis, tuberculoid leprosy, late latent syphilis (treated), 413
- Strawberry Nevil See Angioma
- Strickler, A Polycythemia with unusual eruption, \*172
- Vincent's disease of skin, \*87
- Stubenrauch, C H, Jr Cutaneous neuroma, 202
- Nervus pigmentosus et pilosus, 202
- Sudoriparous Glands See under Sweat Glands
- Sulfadiazine See Coccidioidomycosis, Sulfonamides
- Sulfasuxidine See Sulfonamides
- Sulfathiazole See Fusospirochetosis, Impetigo contagiosa, Sulfonamides
- Sulfonamides, allergy, persistence of desensitization, 412
- fixed bullous eruption due to sulfathiazole, \*342
  - role of inositol in alopecia of rats fed sulfasuxidine, 36
  - skin eruptions due to local application of, 411
  - Therapy See Coccidioidomycosis, Fusospirochetosis, Impetigo contagiosa, Skin, diseases, Syphilis, etc
- Sunlight See Light
- Suprarenal Preparations See Adrenal Preparations
- Suprarenals See Adrenals
- Sutton's Disease See Vitiligo
- Swartz, J H Lichen planus, lichenoid purpuric dermatitis (Gougerot and Blum), avitaminosis A or parapsoriasis, 139
- Sweat Baths See Baths, steam
- Sweat Glands, adenoma of apocrine sweat glands (hidradenoma) of anal canal, 120
- epithelioma, probably arising from sweat glands, 43
  - syringocystadenoma, 45
  - tropical anhidrotic asthenia, 37
  - vasomotor dysfunction associated with hypohidrosis, 69
- Sweltzer, S E Erythema nodosum, 283
- Lymphosarcoma of nose, 287
  - Macular atrophy of buttocks, 284
  - Mycosis fungoides, 286
  - Nodular syphilis, 284
  - Parapsoriasis, case for diagnosis, 284
  - Synovial cyst and psoriasis, 286
  - Tinea circinata, 285
- Sycosis barbae or tuberculosis, 191
- penicillin in civilian practice, 412
- Synovial Membrane, cyst and psoriasis, 286
- synovial pseudocysts, case for diagnosis, 52
- Syphilis late cutaneous or sarcoid, 414
- nodular, 284
  - pseudocarcinomatous hyperplasia in primary, secondary and tertiary cutaneous syphilis, 186
- Syphilis See also Chancre, Neurosyphilis, Syphilis, and under names of organs, regions and diseases
- Bowen's disease of penis, late latent syphilis (treated), 413
  - chemotherapy of, 406
  - congenital acute glomerular nephritis in infant with, 405
  - congenital penicillin in treatment of infantile congenital syphilis, 408

- Syphilis—Continued**  
 early acute yellow atrophy of liver in, case report with summary of literature, 120  
 early, intensive arsenotherapy of \*147  
 early, intensive treatment, method of Eagle and Hogan 410  
 early, intensive treatment with oxophenarsine hydrochloride by multiple injections, \*155  
 early, penicillin in treatment of early syphilis resistant to arsenic and bismuth, 405  
 extragenital syphilitic infection in Negroes, \*114  
 fever and sterile abscess formation accompanying treatment of syphilis with penicillin, \*399  
*Hereditary* See Syphilis, congenital  
 infectious granuloma (tuberculous, syphilitic), 210  
 late, case for diagnosis, 111  
 lichen syphiliticus (extragenital infection) or lichen scrofulosorum, 195  
 nodular interstitial glossitis due to 277  
 postsyphilitic dyschromia, late dyschromic pinta (treated), 115  
 recurrent, macular atrophy secondary to syphilis, 212  
 relation of eye to immunity in experimental syphilis, development of immunity after primary intracorneal inoculation influence of nonspecific inflammatory reaction in cornea on development of immunity in that tissue after intratesticular inoculation, 121  
 review of recent literature 106  
 sarcoid late secondary syphilis 216  
 sarcoidosis tuberculoid leprosy, late latent syphilis (treated) 413  
 secondary or parapsoriasis 213  
 subliminal mass in treatment of 406  
 spirochetal action of penicillin in vitro and its temperature coefficient 408  
 syphilitic juxta-articular nodules combined with leukoderma of wrists, palms and feet, 66  
 tertiary, gumma of palate, 69  
 transmitted from congenitally syphilitic child to his own father, 272
- Syphilid** See Syphilis
- Syphilology** American Board of Dermatology and Syphilology 70, 269  
 eligibility requirements for examination by American Board of Dermatology and Syphilology, Inc 428
- Syringocystadenoma**, 45
- Tabes Dorsalis** See also Neurosyphilis  
 dermatofibrosarcoma protuberans with dementia paralytica tabetic type, 202
- Targan N A** Ringworm of eyebrow \*116
- Tasker S** Colloid degeneration of skin (colloid milium), report of case with observations on ascorbic acid \*180  
 Dermatitis medicamentosa associated with secondary polycythemia, report of case \*389
- Teaching** See Education
- Teeth**, development, ectodermal dysplasia with partial anodontia, 272
- Telangiectasia** See also Angioma, Purpura annularis telangiectodes  
 diffuse, of trunk and upper extremities case for diagnosis, 124
- Temperature** urticaria pigmentosa with sensitiveness to 190
- Testosterone** See Androgens
- Thermotherapy**, action of electric blankets, 37
- Thiamine** See also Vitamins, B  
 chickenpox, herpes zoster and acute anterior polymyositis, 410
- Thorax** match dermatitis on chest and secondary and grease allergy of face, 68  
 papulonecrotic tubercula including involvement of face, chest and back, 205
- Thrombocytopenia** See Purpura
- Thrush** See Moniliasis
- Thurmon F M** Dermatitis medicamentosa, case for diagnosis, 139  
 Morphea, case for diagnosis, 139
- Ticks** See Tularemia
- Timbó** See Lonchocarpus
- Tinea** See also Microsporosis, Ringworm  
 Amlantacea See Seborrhea  
 capitis 56  
 cillorum and tinea corporis, 426  
 circinata, 285  
 corporis and tinea cillorum, 426  
 Decalvans See Alopecia areata  
 undecylenic acid in treatment of dermatomycosis, \*166  
 versicolor, pityriasis versicolor in South Pacific, \*75
- Tissue**, penetration of surface tissues with copper by iontophoresis, penetration with organic and inorganic copper salts and use of detergents in iontophoresis, \*96  
 semblance of elastic tissue to mycelium in potassium hydroxide preparations, \*115, 401
- Tobias N** Scrotal tongue and its inheritance, \*266
- Toe Nails** See Nails
- Toes** See Fingers and Toes
- Tolmich J A** Localized myxedema 211
- Tongue** nodular interstitial glossitis due to syphilis, 277  
 scrotal, and its inheritance \*266  
 tumor case for diagnosis, 282
- Torrey, F A** Ichthyosiform erythroderma, 130
- Toxicodermas** See Dermatitis, venenata
- Traub F F** Keloid following herpes zoster 203  
 New cutaneous bactericidal agent used in soap, further practical studies \*385  
 Possible lupus erythematosus, 128
- Trench Foot** See Foot
- Treponema Pallidum** See Syphilis
- Treponematoses** See Frambesia, Syphilis
- Trichophyton purpureum** onychomycosis due to, 124  
 rubrum onychomycosis and dermatomycosis caused by Trichophyton rubrum and Aspergillus nidulans, \*162  
 treatment of pityriasis rosea with Trichophyton extract 184
- Trichophytosis** See also Mycosis, cutaneous  
 and generalized moniliasis, 277  
 barbae, 419
- Tropical Medicine** See also under names of tropical diseases as Leishmaniasis, Ulcers tropical, etc  
 acne vulgaris occurring in tropics in pigmentary and pilosebaceous nevus \*322  
 clinical investigation of new cutaneous entity, \*226  
 course in tropical dermatology 70 268  
 cutaneous diseases in South Pacific, observations among military forces, \*75  
 dermatologic therapy in tropics, 273  
 impetigo bullosa in tropics \*28 268  
 new cutaneous syndrome occurring in New Guinea and adjacent islands preliminary report \*221  
 skin diseases in tropics 37  
 tropical anhidrotic asthenia 37  
 tropical lichen planus-like disease \*1
- Tropics**, diseases of skin among natives of north-east New Guinea, \*247
- Trow E J** Intensive treatment of early syphilis with oxophenarsine hydrochloride by multiple injections \*155
- Tryparsamide**, neurosyphilis and oculist 121
- Tubercle Bacilli** See also Tuberculosis  
 effect of tuberculous and sensitized sera and serum fractions on development of tubercles in chorioallantoic membrane of chick 408
- Tubercula** See also under Tuberculosis  
 case for diagnosis, 197  
 papulonecrotic including involvement of face, chest and back, 205  
 rosacea-like, of Lewandowsky or rosacea, 41
- Tuberculin** See under Tuberculosis  
 Patch Test See Tuberculosis
- Tuberculosis** See also Tubercula, and under names of diseases organs and regions  
 classification of tuberculosis of skin \*108  
 colligativa and lichen scrofulosorum 189  
 cutis (?) and psoriasis 294  
 effect of tuberculous and sensitized sera and serum fractions on development of tubercles in chorioallantoic membrane of chick 408

- Tuberculosis**—Continued  
 Infectious granuloma (tuberculous, syphilitic), 210  
 Inoculation, 132  
 miliaris disseminata faciei, 59, 203  
 or sycosis barbae, 191  
 pulmonary, and parapsoriasis, 45  
 pulmonary, tuberculosis verrucosa cutis in patient with advanced pulmonary tuberculosis, 136  
 sensitivity of tuberculin patch test (Vollmer-Lederle), results with 318 persons presenting various dermatoses, \*249  
 verrucosa cutis, 68  
 verrucosa cutis in patient with advanced pulmonary tuberculosis, 136
- Tularemia**, infection of ticks (*Dermacentor variabilis*) with *Pasteurella tularensis*, 409
- Tumors** See Adenoma, Angioma, Cancer, Epithelioma, Lymphoblastoma, Melanoma, Neuroma, Papilloma, Sarcoma, etc and under names of organs and regions, as Pancreas, Tongue, etc
- Twining, H E** Chronic blepharitis (cause, therapy?), 192  
 Tuberculosis or sycosis barbae, 191
- Twins** Identical, von Recklinghausen's disease in, 212
- Tythriclein** See Acrodermatitis perstans
- Ulcers** See also under names of organs and regions  
 arsenical keratoses of palms and soles or trophic ulcer of foot, 126  
 case of diagnosis 17  
 salt water ulcers of extremities, occurrence in Japanese survivors, 411  
 Tropical See also Fusospirochetosis, Leishmaniasis  
 tropical in South Pacific, \*75
- Ultraviolet Rays** See also Light  
 relation of ultraviolet-induced mutations to speciation in dermatophytes \*257  
 Therapy See under names of organs, regions and diseases
- Undecylenic Acid** See under Ringworm
- Urbach, E** Carbohydrate metabolism and skin, \*301  
 White cross stripe of finger nails following cardiac infarction \*106
- Urticaria**, beta dimethylaminoethyl benzhydryl ether hydrochloride (Benadril) in treatment, \*239  
 caused by chlorinated drinking water, 272  
 chronic recurrent, 124  
 from perfume \*11  
 pigmentosa 132  
 pigmentosa (acquired type) case for diagnosis, 209  
 pigmentosa with sensitivity to temperature 190  
 urticarial reaction from penicillin 291
- Urushiol** See Rhus, poisoning
- Usher-Seneac Syndrome** See Pemphigus
- Uterus**, chaneroid of cervix 110
- Vaccinia** See Smallpox
- Van Dyck, L S** Alopecia prematura, 126  
 Lupus erythematosus, pityriasis-rosea-like dermatitis following therapy with gold salt, 193
- Varicella** See Chickenpox
- Variolose** Vels cutaneous and subcutaneous lesions of lower limbs in connection with veins, differential diagnosis \*376
- Varicella** See Smallpox
- Vasomotor System** treatment of dermatoses with vasodilators \*344  
 vasomotor dysfunction associated with hypohidrosis 69
- Veins** cutaneous and subcutaneous lesions of lower limbs in connection with veins, differential diagnosis \*376
- Veneral Diseases** See Chancre Chaneroid, Neurosyphilis Syphilis etc
- Verrucae** Immunization therapy of warts, 34  
 plani or lichen planus 192  
 Tuberculosis See Tuberculosis
- Verslon** allergic reactions during administration of penicillin \*93  
 facial lesions due to sulfathiazole \*342  
 vesicular with vesicular eruption \*172  
 vesicular lichen planus or herpes 67
- Vitiligo** See also Albinism  
 chronic recurrent papulopustular dermatitis related to vitamin deficiency, 127
- Vision** See Eyes, accommodation and refraction
- Vitamins** See also Ascorbic Acid, Nicotinic Acid, Thiamine  
 A, disturbances of visual adaptation and their clinical significance, 36  
 A, lichen planus, lichenoid purpuric dermatitis (Gougerot and Blum), avitaminosis A or parapsoriasis, 139  
 A, pityriasis rubra pilaris (vitamin A deficiency), 201  
 A, treatment of ichthyosis, \*178  
 B See also Nicotinic Acid, Pellagra, Thiamine  
 B complex for vitiligo, 117  
 B<sub>1</sub> See Thiamine  
 C See Ascorbic Acid  
 chronic recurrent papulopustular dermatitis related to vitamin deficiency, 127
- Vitiligo** See also Albinism  
 postsyphilitic dyschromia, late dyschromic pinta (treated), 415  
 scleroderma or lichen sclerosis et atrophicus, 140  
 syphilitic juxta-articular nodules combined with leukoderma of wrists, palms and feet, 66  
 vitamin B complex for, 117
- Vollmer-Lederle Test** See Tuberculosis
- Vulva**, amebic infection of vulva complicating granuloma pudendi 273
- Esthiomene** See Lymphogranuloma Venereum
- Walzer, A** Generalized progressive scleroderma with nodules, 210  
 von Recklinghausen's disease in identical twins, 212
- War** See Aviation and Aviators, Military Medicine, Naval Medicine, etc
- Waring, W S** Onychomycosis and dermatomycosis caused by *Trichophyton rubrum* and *Aspergillus nidulans*, \*162
- Warts** See Verruca
- Wassermann Reaction** See Syphilis
- Water**, urticaria caused by chlorinated drinking water, 272
- Waterhouse-Friderichsen Syndrome** See Adrenals, hemorrhage
- Weber, L F** Nevus pigmentosus et pilosus, 202
- Weber-Rendu-Osler's Disease** See Telangiectasia
- Welchsellbium, P K** Rosacea and rhinophyma (nose and ear lobes), 201
- Welding** See Industrial Diseases
- Wetting Agents** See Detergents
- Wheal** See Urticaria
- White Spot Disease** See Scleroderma
- Wilhelm, L F X** Lichen planus or lupus erythematosus, 143
- Wilson, J F** Bromoderma, 191  
 Lichen scrofulosorum and tuberculosis colliquativa, 189  
 Mycosis fungoides exhibiting large concentric lesions and treated with testosterone, 298
- Wilson J W** Improved method for preparing permanent slides of fungus cultures, \*267
- Winer, L H** Periarthritis nodosa, 292
- Winer, M N** Epidermolysis bullosa, suggestion as to possible causation, \*317
- Wise, F** Angiokeratoma (unilateral nevus), 128  
 Angioma, case for diagnosis, 209  
 Angioma or angiosarcoma, 127  
 Diffuse telangiectasia of trunk and upper extremities, case for diagnosis, 124  
 Erythema, 209  
 Papular sarcoid of face, 208  
 Pemphigus case for diagnosis, 218  
 Tuberculosis miliaris disseminata faciei, 203
- Wolf, J** Urticaria pigmentosa, 132
- Wolf, M** Cutaneous and subcutaneous lesions of lower limbs in connection with veins, differential diagnosis \*376
- Wolfe W D** Diseases of the skin among natives of northeast New Guinea, \*247
- Worcester, Noah** one hundredth anniversary of first American textbook of dermatology, 117
- Wright C S** Pemphigus vulgaris improved by acetasone 298  
 Porokeratosis 294  
 Primary inoculation tuberculosis, 293  
 Xanthoma or lipid disturbance, 295



**Xanthelasma** See Xanthoma

**Xanthoma**, effect of feeding lipotropic substance to patients with xanthelasma, \*252  
juvenile xanthomatosis, 191  
or lipid disturbance, 295  
tuberosum, 45

xanthelasma papulosum multiplex, case for diagnosis, 51

**Xanthomatosis** See Xanthoma

**Xeroderma pigmentosum**, additional notes on 6 cases of Dr Mayrand and Dr Gaumond, \*176  
pigmentosum with precocious malignancy, 421

**X-Rays** See Roentgen Rays

**Yaws** See Frambesia

**Zackheim, H S** Use of Benadryl for urticaria and related dermatoses, preliminary report, \*243

**Zakon, S J** Effect of endocrine substances on adult human scalp, \*323  
Urticaria from perfume, \*11

**Zinc chromate**, contact dermatitis due to pigment in zinc chromate primer, 279

chromate, contact dermatitis due to resinous ingredients of zinc chromate primer and certain lacquers, 279

**Zona** See Herpes zoster

**Zycaïne**, dermatitis medicamentosa associated with secondary polycythemia, report of case, \*389

